Review report of MTG8: MiraQ for assessing graft flow during coronary artery bypass graft surgery

This medical technology guidance on MiraQ (MTG8) was published in November 2011.

All medical technology guidance is usually reviewed three years after publication, unless NICE become aware of significant new information before the expected review date.

This review report summarises new evidence and information that has become available since this medical technology guidance was published, and that has been identified as relevant for the purposes of this report. This report will be used to inform NICE's decision on whether this guidance will be updated, amended, remain unchanged (static list) or withdrawn.

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Abbreviations

Term	Definition
ADA	Anterior descending artery
BIMA	Bilateral internal mammary arteries
BITA	Bilateral internal thoracic artery
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CI	Confidence interval
CPB	Cardio-pulmonary bypass
CX	Circumflex artery
DAS	Distal anastomosis support
DF	Diastolic filling
EAC	External Assessment Centre
ECMO	Extra-corporeal membrane oxygenation
EUS	Epicardial ultrasonography
FFR	Fractional flow reserve
GEA	Gastroepiploic artery
GRIIP	Graft Imaging to Improve Patency
HEMS	HyperEye Medical System
IABP	Intra-aortic balloon pump
ICG	Indocyanine green
IFI	Intraoperative fluorescence imaging
iFR	Instantaneous wave-free ratio
ITA	Internal thoracic artery
LAD	Left anterior descending artery
LCA	Left coronary artery
LCX	Left circumflex artery
LDF	Laser Doppler flowmetry
LIMA	Left internal mammary artery
LITA	Left internal thoracic artery
MACE	Major adverse cardiac events
MACCE	Major adverse cardiac and cerebrovascular events
MGF	Mean graft flow
MRI	Magnetic resonance imaging
MTEP	Medical Technologies Evaluation Programme
NuTH	Newcastle upon Tyne Hospitals (NHS Foundation Trust)
OM	Obtuse marginal artery
PCI	Percutaneous coronary intervention
PI	Pulsatility index
PDA	Posterior Descending Artery
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RA	Radial artery

Term	Definition
RCA	Right coronary artery
RCX	Right circumflex artery
RGEA	Right gastroepiploic artery
RIMA	Right internal mammary artery
RITA	Right internal thoracic artery
SITA	Single internal thoracic artery
SV	Saphenous vein
SVG	Saphenous vein graft
TEE	Transoesophageal echocardiography
TTE	Transthoracic echocardiography
TTFM	Transit time flow measurement

1. Original objective of guidance

To assess the clinical and cost-effectiveness of MiraQ for assessing graft flow during coronary artery bypass graft surgery.

2. Current guidance recommendations

From MTG8:

1.1 The case for adopting the MiraQ system in the NHS for assessing graft flow during coronary artery bypass graft (CABG) surgery is supported by the evidence. The evidence suggests that intraoperative transit-time flow measurement is effective in detecting imperfections that may be corrected by graft revision. This may reduce the incidence of graft occlusion and may reduce perioperative morbidity and mortality.

1.2 The MiraQ system is associated with an estimated cost saving of £141 per patient compared with clinical assessment, when it is used routinely for assessing coronary artery bypass grafts during surgery [2018 – see section 5.12].

5.12 For the guidance review, the external assessment centre revised the model to reflect 2017 costs (original guidance values are given in brackets). The main parameter changes were the cost of the MiraQ console £34,000 (£32,000) and probes £1,481 (£1,582) with 50 uses (30 uses). These costs resulted in a MiraQ system cost of about £141 (£111) per procedure. The cost of the time taken to perform a minor revision was estimated to be £24 (£11), and for major revisions, £396 (£180). Treatment costs of post-operative myocardial infarction and associated rehabilitation costs were estimated to be £2,031 (£1,667) per patient and treatment cost by intra-aortic balloon pumping (IABP) was estimated to be £2,574 (£2,657) per episode. Base case results for the 2017 revised model shows the cost saving associated with the MiraQ system was £141 (£115) per patient.

Further details of the 2017 revised model are in the revised model summary [2018].

Additional relevant guidance is described in Appendix A.

3. Methods of review

NICE Information Services repeated the original search strategy used for MTG8 (searches conducted between 30/07/2021 and 02/08/2021), Appendix B. The IS search identified 153 references, reducing to 95 references after deduplication, and shared a reference library (in standard research information system, RIS, format) with the EAC.

The EAC reviewed the literature results against the original scope (NICE MTG8 Scope, 2011), with clarifications sought from both the Company and the Clinical experts, see Appendix C1 and Appendix C2 respectively. Additional detail of the scope included the following:

- Population: patients undergoing CABG surgery, including variants of the procedure: on-pump CABG, off-pump CABG, sequential and composite grafting, multiple arterial grafting, minimal access multivessel CABG, CABG conducted alongside concomitant cardiac procedures (for example valve replacement, carotid endarterectomy). Robotic CABG was considered out of scope.

- Intervention: Transit-time flow measurement (TTFM) devices by Medistim including MiraQ, its predecessors (VeriQ, Butterfly, CardioMed), model variants (SonoQ, VeriQC) and compatible probes (QuickFit) are all included in this review due to equivalent mode of action (Appendix C1). In line with the original assessment report, the endocardial ultrasound component was deemed out of scope. Two Clinical experts confirmed that they were not aware of any competitor devices with the same mode of action. However, published evidence on another device capable of conducting TTFM, Transonic, was identified. The EAC contacted the corresponding authors of papers where the TTFM device was not explicitly reported, for formal confirmation of the intervention. Papers where the TTFM device was

confirmed as Medistim TTFM device were included in this review. Papers where the corresponding author did not respond were excluded from this review.

- Comparator: all studies single-arm and comparative studies reporting the use of the TTFM intervention were included. For the measurement accuracy outcome, studies comparing TTFM with an intraoperative comparator were deemed the most relevant. For the long-term morbidity and mortality outcome measure, comparative studies were deemed the most relevant.

- Study design: letters, editorials, case reports, case series with fewer than ten patients were excluded. Conference abstracts were only included if they were comparative studies.

- Outcomes: long-term results were defined as outcomes from one year and beyond (as recommended by one Clinical expert Appendix C2).

A total of 95 titles and abstracts were sifted by a single reviewer (KK) and 69 were found to be potentially within the scope of the original guidance (NICE MTG8 Scope, 2011). The full text articles for all 69 studies were retrieved and assessed for inclusion against the scope by a single reviewer (KK). A total of 33 were excluded on full text review (Appendix D1). A summary of the sifting and selection process of the EAC literature search is reported in Figure 1. The EAC considered a total of 36 papers from the independent literature search in scope.

The Company provided a spreadsheet containing references of 161 articles (identified though Google Scholar and Pubmed, with the list updated after the yearly clinical evaluation update required for class III medical devices, Appendix C1). The Company submitted references reporting the use of MiraQ or VeriQ published between 2016 and mid-September 2021 (including 105 clinical studies, 29 meta-analyses or reviews, 6 guidelines, expert opinions or editorials, 17 case reports and 4 miscellaneous or other publication types). The Company sent an additional systematic review (Gaudino *et al.* 2021) on 06/10/2021. Note that only 32% (52 of 162) of the studies identified by the

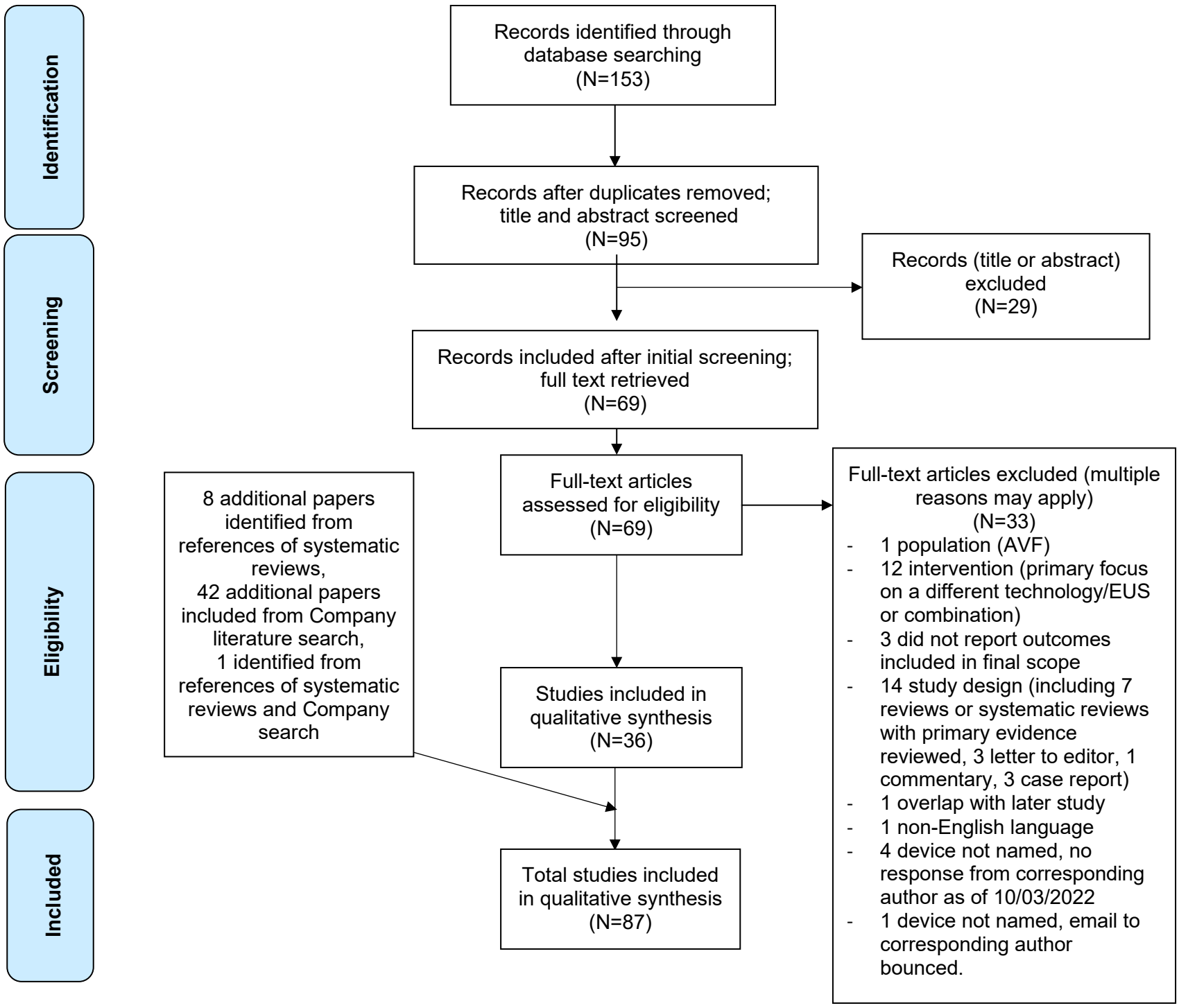
Company search were also identified by the literature search conducted by the NICE IS team. The EAC reviewed the remaining 110 papers (using the same inclusion/exclusion criteria as applied to the NICE literature search), of which 67 were excluded Appendix D2; and 43 studies were subsequently included into this evidence review. An additional 9 studies were identified from references of systematic reviews.

The EAC excluded five studies that did not explicitly report the device or manufacturer used to conduct TTFM (Jia *et al.* 2021; Li *et al.* 2019; Mao *et al.* 2020; Noda *et al.* 2021; Zientara *et al.* 2019). The corresponding author of all five were contacted by the EAC (between 17/02/2022 and 03/03/2022) and no responses have been received by 18/03/2022.

Four studies reported on data from the "REgistry for QUality assESsmenT with ultrasound imaging and TTFM in cardiac bypass surgery" (REQUEST) (Leviner *et al.* 2021; Rosenfeld *et al.* 2021a; Rosenfeld *et al.* 2021b; Taggart *et al.* 2020); however, this used a combination of high-frequency ultrasound and TTFM intraoperatively and none reported outcomes specific to TTFM only and therefore were excluded from this review.

A total of 87 studies were included by the EAC in this review. Of these, twenty-six studies (30%) which were published before 2018, were not considered during the previous evidence review.

Figure 1: PRISMA diagram illustrating EAC literature search



New evidence

3.1 Changes in technology

The two Clinical experts were unaware of newer versions of the technology. The Company confirmed that the technology has not changed since 2011.

3.2 Changes in care pathways

Collated Expert Advice Questionnaires sent from NICE, summarising responses from two Clinical experts, confirms that the care and clinical pathway have not substantially changed since the original assessment. One expert stated that intraoperative flowmetry is standard of care within their department due to complications associated with early graft occlusion. However, one expert stated that due to budget constraints funding the maintenance and replacement of non-essential equipment is difficult. The two experts were not aware of other products with the same purpose as MiraQ.

Published evidence on another device capable of conducting TTFM, Transonic, was identified. The company's submitted evidence included this device. The EAC excluded papers which did not report outcomes exclusively on the Medistim device.

ESC/EACTS Guidelines on myocardial revascularisation (2018) state that TTFM is the most frequently used technique for graft assessment. The guidelines reference two non-comparative studies, which reported between 2 and 4% of grafts required revision due to inadequate flow as highlighted by TTFM. The guidelines state that observational studies have shown TTFM to reduce the rate of adverse events and graft failure, however stated that interpretation can be challenging in sequential and T-graft configurations.

3.3 Results from the Medical Technologies Evaluation Programme research commissioning workstream

The EAC is not aware of any research commissioned by the Medical Technologies Evaluation Programme (MTEP) to inform the guidance review.

3.4 New studies

A total of 87 studies (study characteristics reported in Appendix D3), were deemed in scope by the EAC (additional detail in Appendix D4) including:

- 9 RCTS (in which TTFM was used in both arms rather than as the intervention or comparator);
- 2 subgroups of patients from an RCT;
- 76 cohort studies (including 1 with a control group, and 6 with propensity matching).

Two studies were available as pre-prints only (Urbanowicz *et al.* 2021; Zhao *et al.* 2020b), and only one comparative conferenace abstract was included (Laali *et al.* 2021).

Studies ranged in size between n=12 (Martinovic *et al.* 2019) and n=4,406 (Vrancic *et al.* 2019) patients; one study did not report sample size (Girish Gowda *et al.* 2019). The largest study (Vranci *et al.* 2019) was a retrospective database review which compared in-hospital and follow-up (median 5.1, SD 3.9 years) mortality rates in male and female patients, with sub-stratification analysis according to age. Patients undergoing single or bilateral internal thoracic artery grafts were propensity matched to investigate sex as a significant predictor of late mortality. All patients underwent TTFM during CABG procedure with no comparator reported.

A total of three studies were conducted exclusively in a UK NHS setting (Amin *et al.* 2019; Amin *et al.* 2018a; Amin *et al.* 2018b); two of which were non-comparative cohort studies from a single centre which reported on the need for graft revision (where findings may not be generalizable across the wider

NHS), and the remaining paper reported on measurement accuracy of TTFM with quantitative free-flow measurements (which one Clinical expert stated is not routinely conducted in the NHS).

One study included a high proportion of patients undergoing redo CABG procedures (Rufa *et al.* 2020). Severity of coronary artery disease (CAD) varied across studies. Some studies included patients with severe and diffuse CAD, where patients underwent coronary endarterectomy as an adjunct to CABG (Shehada *et al.* 2019).

Only one study reported in-hospital CABG outcomes with and without TTFM (Laali *et al.* 2021); this was a cohort study available in abstract form only.

Comparative evidence included quantitative assessment of graft flow (however one expert has confirmed that qualitative free flow is the standard of care in the NHS not quantitative), Doppler ultrasonography, coronary angiography, CT angiography, dynamic CT angiography, multi-slice CT angiography and MRI phase-contrast measurement of flow (more detail provided in Appendix D4). Three additional studies used TTFM as the comparator representing standard of care, with the intervention of interest being pre- and post-operative transoesophageal echocardiography, quantitative ICG via the HyperEye Medical System and high-resolution near-infrared angiography. The majority of studies also included other imaging techniques alongside TTFM but did not undertake any comparison of results with VeriQ or MiraQ, included additional statistical analysis of TTFM results and conducted a variety of subgroup analysis (more detail provided in Appendix D4).

Different TTFM thresholds were included across the literature to define graft failure, Table 1.

Table 1: Pre-specified parameters of TTFM used to define graft failure in CABG

Parameter	Value	Study
Mean graft flow	<10 ml/min	Une *et al.* 2013 Yamamoto *et al.* 2022
	≤10 ml/min	Tang *et al.* 2021 Yamamoto *et al.* 2017
	<15 ml/min	Handa *et al.* 2016 Harahsheh *et al.* 2012 (left sided grafts)
	≤15 ml/min	Acipayam *et al.* 2015 Han *et al.* 2021 Zhang *et al.* 2020 Zhang *et al.* 2021 Zhao *et al.* 2020a Zhao *et al.* 2020b
	<20 ml/min	Amin *et al.* 2018a (vein grafts) Amin *et al.* 2019 An *et al.* 2019 Gao *et al.* 2021 (IMA) Harahsheh *et al.* 2012 (RCA) Hiraoka *et al.* 2017 (ITA grafts) Lee *et al.* 2020 Mahmoud *et al.* 2017 Niclauss *et al.* 2020
	≤20 ml/min	Honda *et al.* 2015 Nakajima *et al.* 2018 Nakajima *et al.* 2019 Seetharama Bhat *et al.* 2019 Tolegenuly *et al.* 2020 (IMA grafts) Yuan *et al.* 2018
	<30 ml/min	Stastny *et al.* 2021 Shehada *et al.* 2019
	30-40 ml/min	Amin *et al.* 2018a (vein grafts)
	<40 ml/min	Amin *et al.* 2018a Gao *et al.* 2021 (SVG) Hiraoka *et al.* 2017 (SVG)
	≤40 ml/min	Tolegenuly *et al.* 2020 (SVG)
Pulsatility index	>3	Amin *et al.* 2018a Honda *et al.* 2015 Joshi *et al.* 2020 Stastny *et al.* 2021
	≥3	Ucak 2020
	≥3.5	Niclauss *et al.* 2020
	≥5	Acipayam *et al.* 2015 Erdem *et al.* 2015 Han *et al.* 2021 Harahsheh *et al.* 2012 Seetharama Bhat *et al.* 2019 Shehada *et al.* 2019 Yamamoto *et al.* 2017 Zhang *et al.* 2020 Zhang *et al.* 2021 Zhao *et al.* 2020a Zhao *et al.* 2020b
	>5	Amin *et al.* 2019 An *et al.* 2019 Amin *et al.* 2018a

Parameter	Value	Study
		Dayan *et al.* 2018 Gao *et al.* 2021 Hiraoka *et al.* 2017 Handa *et al.* 2016 Honda *et al.* 2019a Kaya *et al.* 2018 Lee *et al.* 2020 Tolegenuly *et al.* 2020 Une *et al.* 2013 Vechersky *et al.* 2019 Yuan *et al.* 2018
Diastolic filling index	<25%	Honda *et al.* 2015 Tolegenuly *et al.* 2020
	≤25%	Ucak 2020
	<50%	Amin *et al.* 2018a (right sided grafts) Handa *et al.* 2016 Joshi *et al.* 2020 Kaya *et al.* 2018 Une *et al.* 2013
	≤50%	Erdem *et al.* 2015 Han *et al.* 2021 Harahsheh *et al.* 2012 Seetharama Bhat *et al.* 2019 Yamamoto *et al.* 2017
	<60%	Amin *et al.* 2018a (left sided grafts)
Systolic reverse flow	≥3%	Honda *et al.* 2015 Ucak 2020
	>3%	Amin *et al.* 2018a Tolegenuly *et al.* 2020

A summary of outcomes reported across the 87 included studies is shown in Appendix D5. Given the heterogeneity across the included 87 studies, in terms of patient characteristics, CABG procedure technique, graft type, presence of concomitant procedures and variation in definition of graft failure, the EAC considered it inappropriate to conduct meta-analysis.

Proportion of patients with graft failure

A total of 49 studies reported on graft failure, Table 2; with 6 studies reporting on intraoperative outcomes, 17 reporting on early follow-up (between post-operative and up to 2 weeks), 8 reporting on medium-term follow-up (between 1 month and up to 1 year) and 18 reporting on long-term follow-up (1 year and beyond, with maximum follow-up reported of 102.2 months or 8.5 years). However, the EAC notes that some studies reported at multiple time-points. The denominator was reported differently across the included studies; 17 studies reported graft failure per patient (between 0% and 40%), 25 studies reported graft failure per graft (between 0% and 21.9%) and 11 studies reported graft failure per anastomosis (between 0.5% and 13.5%). Differences

in graft failure between studies may be related to differences in patient populations (disease severity, comorbidities, medication), intervention (grafts used, on/off-pump, concomitant procedures), definition of failure (including different imaging to confirm patency or failure) and the graft failure outcome being measured at different time points. Due to study heterogeneity, the EAC has not conducted meta-analysis.

Table 2: Summary of 49 studies reporting on graft failure/defects

				Failure		
#	Study (year)	Time point	Outcome assessment method	%, per patient	%, per graft	%, per anastomosis
1.	Harahsheh *et al.* 2012	Intraoperative	N/A	-	7.2% (100/1394)	-
2.	Kornovski *et al.* 2017	Intraoperative	N/A	-	2.5% (4/161)	-
3.	Shehada *et al.* 2019	Intraoperative	Coronary or multi-slice CT angiography	3.6% (4/112)	-	-
4.	Stastny *et al.* 2021	Intraoperative	Epicardial ultrasound	0% (0/134)	-	-
5.	Tolegenuly *et al.* 2021	Intraoperative	CT angiography	44% (22/50)	2.1% (3/144)	10.6% (17/160)
6.	Tolegenuly *et al.* 2020	Intraoperative	Coronary angiogram	-	1.1% (1/89)	-
7.	Chang *et al.* 2018	Postoperative (1.1 days†)	Coronary angiography	-	-	7.0% (6/86)
8.	Hosono *et al.* 2020	Post-operative	Coronary or multi-slice CT angiography	-	-	-
9.	Han *et al.* 2021	Post-operative to discharge (no exact timeframe given)	CT angiogram	0% (0/74)	-	
10.	Hwang *et al.* 2018	Postoperative	Coronary angiography	-	-	2.4% (2/85) - left ITA: 0% (0/29) - SVG: 3.6% (2/56)
11.	Kim *et al.* 2021	Postoperative	Coronary angiography	-	-	1.2% (56/4518) - ITA: 0.1% (1/1259) - SVG: 1.7% (55/3260)
12.	Kim *et al.* 2020	Post-operative (1.5 days†)	Coronary angiography	-	1.8% (165/9001) - 2.8% (42/672) - 1.5% (123/8329)	-
13.	Nakajima *et al.* 2016	Postoperative	CT or coronary angiography	-	0% (0/47)	-
14.	Nakajima *et al.* 2018	Postoperative	Coronary angiography	-	6.4% (47/736) - pPCI: 9.2% - no pPCI: 1.8%	-
15.	Benetti *et al.* 2021	Discharge (mean 60 hours post-op)	N/A	0% (0/16)	-	-
16.	Davierwala *et al.* 2021a	Discharge	Coronary angiography	-	-	3.2% (4/124)
17.	Jiang *et al.* 2020	Discharge (mean 6 days post-op)	Multi-slice CT angiography	0% (0/59)	-	-
18.	Zhang *et al.* 2021	Discharge	CT angiography	-	3.5% (27/761)	-
19.	Zhang *et al.* 2020	Discharge	CT angiography	-	1.3% (5/390) - LIMA: 1.3% (4/313) - RIMA: 3.0% (1/34) - SVG: 0% (0/40)	-
20.	Zhao *et al.* 2020b	Discharge	CT angiography	1.1% (4/356) - LIMA: 1.3% (4/313) - SVG: 0% (0/42)	-	-
21.	Kuroyanagi *et al.* 2012	1 week	Coronary or CT angiography	-	0.5% (2/435)	0.5% (3/578)
22.	Zhao *et al.* 2020	1 week	CT angiography	-	3.8% (12/310)	-
23.	Tamura *et al.* 2021	Within 14 days	Coronary angiography	-	5.1% (15/293) - open harvest: 5.3% (12/225) - endoscopic harvest: 4.4% (3/68)	-
24.	Oshima *et al.* 2016	1 month	Coronary angiography	-	7.0% (15/214)	-
25.	Yamamoto *et al.* 2022	1 month	Coronary or CT angiography	14% (6/43)	-	-
26.	Nakajima *et al.* 2019	1.5 months†	Coronary angiography	12.2% (28/230)	-	-
27.	Guo *et al.* 2019	3 months	CT angiography & Doppler echocardiography	-	NR - Arterial: 1.9% (3/155) - Venous: 3.2% (5/155)	-
28.	Hiraoka *et al.* 2017	3 months	Multi-slice CT angiography	-	8.7% (9/104)	-
29.	Pettersen *et al.* 2017	6 months	CT angiogram	-	-	10% (10/100) - conventional vein: 12% (6/50) - pedicled vein: 8% (4/50)
30.	Honda *et al.* 2015	213 days	Multi-slice CT angiography (n=65), MRI (n=2), coronary angiography (n=2)	1.4% (1/69)	-	-
31.	Tolegenuly *et al.* 2021	224 days†	CT angiography	0% (0/48)	-	-
32.	An *et al.* 2019	1 year	CT angiography	-	9.9%† - 0.5%† (1/212)	-
33.	Chang *et al.* 2018	1 year	Coronary angiography	15.4% (4/26)	-	1.1% (1/94)
34.	Handa *et al.* 2016	1 year	Coronary angiography	-	21.9%† (25/114)	-
35.	Inderbitzin *et al.* 2015	1 year	CT angiography	-	10%† (5/50)	-
36.	Li *et al.* 2021a	1 year	Multi-slice CT angiography	-	-	13.5%† - LAD: 9.9%† - Cx: 9.8%† - RCA: 20.7%†
37.	Mohamed *et al.* 2019	1 year	Coronary and CT angiography	33.3% (4/12)	-	-
38.	Monsefi *et al.* 2016	1 year	Multi-slice CT angiography	6.7% (3/45)	-	-
39.	Tamim *et al.* 2020	1 year	Multi-slice CT angiography	10.0% (5/50)	-	- RA: NR - LIMA: 3.7% (2/54)

#	Study (year)	Time point	Outcome assessment method	Failure		
				%, per patient	%, per graft	%, per anastomosis
						- RIMA: 0% (0/11) - SVG: 18.7% (14/75)
40.	Tang *et al.* 2021	1 year	Multi-slice CT angiography	-	7.1% (34/477)	-
41.	Une *et al.* 2013	1 year	Coronary or multi-slice CT angiography	-	20.8% (22/106) - Arterial: 0% (0/41) - SVG: 33.8% (22/65)	-
42.	Hwang *et al.* 2018	13 months†	Coronary or multislice CT angiography	-	-	9.2% (7/76) - left ITA: 4.0% (1/25) - SVG: 11.8% (6/51)
43.	Yuan *et al.* 2018	26.5 months†	Coronary or CT angiography	-	NR - LIMA: 0% - RIMA: 3.3% - RA: 6.9% - RGEA: 12.5%	-
44.	Dreifaldt *et al.* 2013	3 years†	Coronary angiography	-	12.1% (24/198) - Arterial: 18.2% (18/99) - NT-SVG: 6.1% (6/99)	-
45.	Li *et al.* 2021b	3 years	Coronary or CT angiography	17.5% (34/194) - 15.4% (16/104) - 23.4% (22/94)	-	-
46.	Shehada *et al.* 2019	53 months†	Coronary or multi-slice CT angiography	-	11.0% (52/474) - non-CEA: 9.6% (32/335) - CEA: 14.4% (20/139)	-
47.	Yuan *et al.* 2018	68.3 months†	Coronary or CT angiography	-	NR - LIMA: 4.9% - RIMA: 6.4% - RA: 10.0% - RGEA: 12.5%	-
48.	Bazylev *et al.* 2018	6 years	Coronary angiography	23.5%	-	-
49.	Yuan *et al.* 2018	102.2 months†	Coronary or CT angiography	-	NR - LIMA: 6.4% - RIMA: 8.3% - RA: 13.0% - RGEA: 33.3%	-

Abbreviations: ADA, anterior descending artery; CEA, coronary endartectomy; CT, computed tomography; Cx, circumflex artery; DAS, distal anastomosis support; LAD left anterior descending branch; LIMA, Left internal mammary artery; NT-SVG, no-touch saphenous vein graft; pPCI, prior percutaneous coronary intervention; RCA, right coronary artery; RGEA, Right gastroepiploic artery SVG, saphenous vein grafts; TTFM, transit-time flowmetry; †mean

Time to graft failure

The majority of studies (43/49, 88%) reported on graft failure post-operatively, Table 2. However, only two studies (both non-comparative studies, where intraoperative TTFM was used in all patients) used Kaplan-Meier analysis for time to graft failure accounting for different length of follow-up across patients and censoring. Bazylev *et al.* (2018) included 17 patients with a follow-up period of 72 months and reported 4 occluded grafts in the group of patients in whom ligation of the ADA was not performed (n=8) however did not provide the proportion or 95% confidence intervals of graft failure at specific event time points. Yuan *et al.* (2018) reported that patency of four graft types (LIMA, RIMA, RA, and RGEA) decreased over time, however the number of patients with each graft type, proportion and 95% confidence intervals at specific time points were not explicitly reported.

Peri- and post-operative clinical events associated with graft failure (including mortality)

Only one conference abstract reported outcomes directly compared peri- and post-operative clinical events in patients receiving TTFM (n=433) with *different* non-randomised patients not receiving TTFM (n=492) alongside cardio-pulmonary bypass (CPB) procedures (Laali *et al.* 2021). Authors reported on the occurrences of major adverse cardiac events (MACE) including in-hospital cardiac mortality, perioperative myocardial infarction, cardiac arrest and the need for extra-corporeal membrane oxygenation (ECMO). MACE outcomes were significantly different with fewer adverse events occurring in patients receiving TTFM (n=9, 2.1%) and those not (n=28, 5.7%) ($p<0.01$). The proportions of perioperative myocardial infarction, postoperative cardiac arrests, need for ECMO, and in-hospital cardiac and overall mortality were fewer in the group receiving TTFM to those not, however these were not statistically different. Preoperative characteristics between groups were not significantly different aside from lower levels of extra-cardiac arteriopathy in those receiving TTFM (n=39, 9%) compared to those not (n=83, 17%) ($p<0.001$). However, the EAC notes that this study was not powered to detect differences in these outcomes, and did not account for multiple statistical tests.

Of the remaining included evidence, 16 comparative and 41 single-arm studies reported on peri- and post-operative clinical events. The comparative evidence included a range of interventions and comparators including concomitant pharmaceutical interventions or surgical techniques with all patients receiving TTFM. Due to the lack of comparative data comparing those receiving TTFM and those not, these are considered as single-arm studies for this outcome and have not been summarised by the EAC.

Frequency of need for graft revision (including repeat coronary revascularisation)

The EAC notes that the total revision rate used in the original Company economic model was on a per patient basis, however the type of revision (major or minor) was on a per graft basis. Hence, the EAC has reported both denominators when summarising the new evidence. The EAC reported type of revision (redo CABG, PCI, other cardiac surgery) only if reported in the study.

A total of 38 studies reported on this outcome, Table 3; 10 of which stated no revisions. Of studies reporting the proportion of patients or procedures requiring revision, a total of 11 studies reported on intra-operative revision (range between 0% and 11.6%), 11 studies reported on early outcomes post-operatively up to 1 year after CABG surgery (between 0% and 5.7%) and 9 studies reporting on late outcomes from follow-up at 1 year or later (between 0% and 9.6%).

Table 3: Summary of 38 studies reporting on revision

#	Study (year)	Time point	Revision		
			% (per procedure or patient)	% (per graft)	% (per anastomoses)
1.	Acipayam *et al.* 2015	Intra-operative	-	0% (NR)	-
2.	Amin *et al.* 2019	Intra-operative	-	5.8%[α] (15/257)	-
3.	Amin *et al.* 2018a	Intra-operative	0% (0/35)	-	-
4.	Davierwala *et al.* 2021a	Intra-operative	5.7% [β] (5/88)	-	-
5.	De Leon *et al.* 2020	Intra-operative	-	0.9% (5/543)	-
6.	Driedfaldt *et al.* 2013	Intra-operative	0% (0/99)	-	-
7.	Harahsheh *et al.* 2012	Intra-operative	1.1% (5/436)	-	-
8.	Hashim *et al.* 2018	Intra-operative	3.3% (2/60)	-	-
9.	Jiang *et al.* 2020	Intra-operative	8.5% (5/59)	-	-
10.	Joshi *et al.* 2020	Intra-operative	2.5% (1/40)	-	-
11.	Kaya *et al.* 2018	Intra-operative	11.5% (143/1240)	4.1% (146/3596)	-
12.	Kim *et al.* 2020	Intra-operative	5.6% (150/2685)	-	-
13.	Kuroyanagi *et al.* 2012	Intra-operative	-	-	2.1% (12/578)
14.	Laali *et al.* 2021	Intra-operative	1.2% (5/433)	-	-
15.	Seetharama Bhat *et al.* 2019	Intra-operative	11.6% (49/424)	4.2% (51/1203)	-
16.	Tolegenuly *et al.* 2021	Intra-operative	-	6.9% (10/144)	-
17.	Tolegenuly *et al.* 2020	Intra-operative	-	1.1% (1/89)	-
18.	Vechersky *et al.* 2019	Intra-operative	-	4.2% (9/214)	-
19.	Erdem *et al.* 2015	Post-operative (at least 24h)	5.7% (8/140)	-	-
20.	Rufa *et al.* 2020[K]	Post-operative	1.6% (5/304) 0.3%[β] (1/304)	-	-
21.	Kim *et al.* 2020	Discharge (mean 1.5 days post-op)	2.7%[§] (76/2820) - Pre-TTFM: 7.2% (16/211) - Post-TTFM: 2.3% (60/2599)	-	-
22.	Benetti *et al.* 2021	Discharge (mean 60 hours)	0% (0/16)	-	-
23.	Cerqueira Neto *et al.* 2012	Follow-up (30 days)	0% [β] (0/35)	-	-
24.	Gao *et al.* 2021	Follow-up (3 months)	0% (0/52)	-	-
25.	Guo *et al.* 2019	Follow-up (3 months)	0%[α] (0/155)	-	-
26.	Hiraoka *et al.* 2017	Follow-up (3 months)	0% (0/63)	-	-
27.	Pettersen *et al.* 2017	Follow-up (6 months)	1.7%[β] (1/60)	-	-
28.	Honda *et al.* 2015	Follow-up (10 months)	1.4% (1/72)	-	-
29.	Davierwala *et al.* 2021a	Follow-up (10.5 months†)	1.2%[β] (1/82)	-	-
30.	Mohamed *et al.* 2019	Follow-up (1 year)	8% (4/50)	-	-
31.	Hiraoka *et al.* 2017	Follow-up (413 days)†	4.8%[β] (3/63)	-	-
32.	Yuan *et al.* 2018	Follow-up (26.9 months†)	0% (0/168)	-	-
33.	Su *et al.* 2018	Follow-up (>35 months†)	1.8% (5/279)	-	-
34.	Monsefi *et al.* 2016	Follow-up (4-years)	0% (0/102)	-	-
35.	Shehada *et al.* 2019	Follow-up (53 months†)	20.7%[β] (18/87) 0%[α] (0/87) 5.7%[¥] (5/87)	-	-
36.	Yuan *et al.* 2018	Follow-up (73.8 months†)	3.6% (5/139)	-	-
37.	De Leon *et al.* 2020	Follow-up (7.8 years†)	9.6%[β] (17/177)	-	-
38.	Yuan *et al.* 2018	Follow-up (109.6 months†)	8.7% (13/150)	-	-

Abbreviations:
*Note only 1/160 (0.6%) required revision based on TTFM
[α] Repeat CABG
[β] Defined as PCI
[§] Includes PCI
[¥]other cardiac surgery
[K]redo CABG

The EAC also identifed one study (Seetharama Bhat *et al.* 2019) that reported and compared pre- and post-revision TTFM measurements. The study stated that a total of 51 of 1203 (4.2%) grafts from 49 patients had abnormal TTFM results (mean graft flow less than 20 ml/min, pulsatility index greater than 5, or diastolic flow less than 50%) and underwent graft revision. Following revision and repeated TTFM measurement, the mean graft flow was significantly higher ($p<0.001$) and pulsatility index was significantly lower ($p<0.001$) than TTFM measurements obtained before the revision. Without a comparator group it is difficult to determine the clinical outcome of these patients had the TTFM not highlighted the need for revision. However, this study does highlight that surgical revision resulted in a significant improvement in both mean graft flow and pulsatility index, bringing them within defined 'normal' thresholds.

Long-term morbidity and mortality

No study reported *long-term* mobidity and mortality in a comparison of patients receiving TTFM to *different* patients not receiving TTFM. Laali *et al.* (2021) reported in-hospital (*short-term*) outcomes across patients receiving TTFM (n=433) and those not receiving TTFM (n=492). Major adverse cardiac events were significantly lower in those receiving TTFM (9 of 433, 2.1% compared with 28 of 492, 5.7%; $p<0.01$) as were post-operative cardiac arrest (3 of 433, 0.7% compared with 12 of 492, 2.4%; $p=0.036$) and in-hospital cardiac mortality (2 of 433, 0.46% compared with 11 of 492, 2.2%; $p=0.022$). The study also reported no significant difference in peri-operative MI (2 of 433, 0.5% compared with 5 of 492, 1.0%; $p=0.46$), need for extra-corporeal membrane oxygenation (8 of 433, 1.8% compared with 15 of 492, 3.0%; $p=0.24$) or in-hospital overall mortality (7 of 433, 1.6% compared with 16 of 492, 3.3%; $p=0.11$) between arms. However, the EAC notes that this study was not powered to detect differences in these outcomes, and did not account for multiple statistical tests.

Measurement accuracy

Four studies reported on measurement accuracy of the Medistim TTFM device, Table 4, relative to an intraoperative comparator.

Two studies compared intraoperative measurements of TTFM and quantitative free flow (Amin *et al.* 2018b; Girish Gowda *et al.* 2019); however one Clinical expert advised that quantitative free flow measurement is not standard NHS practice (Appendix C2). Amin *et al.* (2018b) reported a strong correlation of r=0.89 in flow rates between TTFM and free-flow. Bland-Altman analysis showed that TTFM technique may underestimate at low flows and overestimate at higher flows. TTFM technique systematically overestimated the average of TTFM and free flow during prevasodilation by 7.1% (SD 16.3%, p=0.0012). The study reported no systematic difference in flow after vasodilation, and that overestimation of flow was more common with 4mm TTFM probes. Girish Gowda *et al.* (2019) also reported that TTFM overestimated flow rate, with a mean difference of 8.8 ml/min (TTFM – free flow), however limits of agreement were wide (between -2.3 ml/min and +19.8 ml/min).

Hellmann *et al.* (2020) reported a significant positive correlation between myocardial perfusion as assessed by laser Doppler flowmetry with mean graft flow as assessed by TTFM in 26 patients; r=0.521 (p=0.002).

Yamamoto *et al.* (2017) reported significant differences in mean graft flow, pulsatility index and diagnostic filling percentage between 66 patent and 9 failed internal thoracic artery grafts, as determined by post-operative fluoroscopic coronary artery angiography. The study also reported significant differences in mean graft flow, pulsatility index and diagnostic filling percentage between 93 patent and 9 failed saphenous vein and radial artery grafts. A moderate correlation was reported between the average acceleration (derived from the results of the luminance intensity measurements from the HyperEye Medical Systems using intraoperative indocyanine green) and the mean graft flow (ITA r=0.570; SV/RA r=0.600); however p-values were not reported. No significant correlation was found between mean graft flow and time to peak intensity.

Table 4: Summary of N=4 studies reporting measurement accuracy of TTFM with intraoperative comparator; mean [95% CI], mean (SD)

Study (year)	Intervention	Comparator	Correlation	Bland-Altman (TTFM – comparator)	Receiver operating characteristic (TTFM)
Amin *et al.* (2018b)	TTFM	Free flow (20 s)	0.89	TTFM overestimation: 7.1% (SD 16.3%, p=0.0012). No systematic difference with 3mm probes.	0.76 [95%CI 0.67 to 0.84], p<0.001 Optimal cut-off for TTFM for assuming flow overestimation was 68 ml/min, sensitivity of 71%, specificity 71%.
Girish Gowda *et al.* (2019)	TTFM	Free flow (15 s)	-	8.8 ml/min, LoA: -2.3 to +19.8 ml/min	-
Hellmann *et al.* (2020)	TTFM	Laser Doppler flowmetry	0.521 (p=0.002)	-	-
Yamamoto *et al.* (2017)	TTFM	Coronary angiography with Indocyanine green	0.570 (ITA) 0.600 (SV/RA)	-	-
Abbreviations: ITA, internal thoracic artery; LoA, limits of agreement; RA, radial artery; SV, saphenous vein; TTFM, transit time flow measurement;					

Time taken to generate and record data during operation
Only one conference abstract reported cardiopulmonary bypass times in patients undergoing TTFM (n=433) compared with a different cohort of patients without TTFM (n=492) (Laali *et al.* 2021). The study reported the procedure times were significantly longer with patients treated with TTFM; 82 (SD 24) with TTFM and 78 (SD 25) minutes without TTFM (p=0.023). The study also reported that there was no significant difference in cross-clamp time (p=0.86) and no significant difference in the number of grafts used (p=0.95) between patients receiving TTFM and those not.

Number of probes used per procedure
No studies reported on this outcome.

Number of times each probe can be used
No studies reported on this outcome.

3.5 Ongoing trials
The EAC searched for "MiraQ" or "VeriQ" or "Medistim" on clinicaltrials.gov on 03/02/2022 and identified four studies, all completed; one had multiple publications listed, one was not relevant (liver graft), one was primarily focused on a different device (Echoclip), and the remaining study completed in 2018 but did not include a reference to any publications, Table 5.

Table 5: completed studies identified from clinicaltrials.gov website.

Trial number	Study name	EAC comment
NCT02385344 Completed December 2017	Registry for Quality Assessment With Ultrasound Imaging and TTFM in Cardiac Bypass Surgery (REQUEST)	Three publications listed (using Epicardial Ultrasonography (EUS) and TTFM): • Leviner *et al.* Transit time flow measurement of coronary bypass grafts before and after protamine administration. J Cardiothorac Surg. 2021; 16(1): 195 • Rosenfeld *et al.* Intraoperative transit-time flow measurement and high-frequency ultrasound in coronary artery bypass grafting: impact in off versus on-pump, arterial versus venous grafting and cardiac territory grafted. Eur J Cardiothorac Surg. 2021a; 61(1): 204-213 • Rosenfeld *et al.* Intraoperative surgical strategy changes in patients with chronic and end-stage renal disease undergoing coronary artery bypass

		grafting. Eur J Cardiothorac Surg. 2021b; 59(6): 1210-1217.
NCT02791087 Completed October 2018	Investigation of the Role of Hemodynamics in Re-stenosis of CABG Patients	
NCT02515708 Completed June 2020	Pilot Study to Assess Safety and Feasibility of Normothermic Machine Preservation In Human Liver Transplantation	Population not in scope (liver graft)
NCT02919124 Completed December 2019	Epicardial Echocardiography of Coronary Anastomoses Using the Echoclip Device	Focus on Echoclip device Three publications listed: • Staalsen *et al.* A new technique facilitating intraoperative, high-frequency echocardiography of coronary bypass graft anastomoses. J Thorac Cardiovasc Surg. 2011 Jan;141(1):295-6. • Andreasen *et al.* Peroperative epicardial ultrasonography of distal coronary artery bypass graft anastomoses using a stabilizing device. A feasibility study. J Cardiothorac Surg. 2020 Jan 8;15(1):3. • Andreasen *et al.* A case report on epicardial ultrasonography of coronary anastomoses using a stabilizing device without the use of ultrasound gel. J Cardiothorac Surg. 2019 Mar 13;14(1):59.

3.6 Changes in cost case

The clinical parameters within the original economic model were informed by two clinical experts (Dr Bergsland, oral communication; Dr Kieser, e-mail correspondence) and two published clinical studies:

- Becit *et al.* (2007); retrospective comparative cohort study reporting results of intraoperative TTFM in patients undergoing on-pump isolated CABG (Assessment Report, 2011). The study comprised 2 series each of 100 consecutive patients: Group A included the last 100 patients before TTFM was introduced, and Group B included the first 100 patients after TTFM was introduced at a single centre in Turkey. Graft revision was performed with PI greater than 5 and backward flow less than 50%.

- Kieser *et al.* (2010); cohort study which included 336 consecutive CABG patients and total of 1,000 arterial grafts from a single centre in Canada. Each patient was assessed with TTFM (Medistim).

NICE published a review of MTG8 in 2018, with a costing update. Opinion from two Clinical experts did not suggest any updates to the clinical parameters used in the model update. The EAC have considered the additional evidence identified in this review for each clinical parameter in the updated economic model, Table 6, with reference to the costing update 2021 (EAC MTG8 Costing Update, 2021).

Table 6. Clinical parameters used in the economic model

Variable	Value	Source	EAC comment
Duration of TTFM, per procedure	2.35 minutes	Dr Bergsland, oral communication, and Dr Kieser, e-mail communication	Only one conference abstract identified by the EAC (Laali *et al*. 2021) reported procedure times in patients receiving TTFM to those not. Time was reported as total procedure time, rather than additional time for TTFM, with a mean (SD) time of 82 (24) and 78 (25) minutes with and without TTFM respectively. The EAC have not identified any additional evidence to justify updating this parameter in economic modelling.
Number of probes used per procedure	1.7	Company submission document for VeriQ systems.	The EAC did not identify any studies reporting this outcome; no change to economic model.
Probe uses	50	Company submission document for VeriQ systems.	The EAC did not identify any studies reporting this outcome; no change to economic model. Costing update assumed a probe lifespan of 50 uses with a mean of 1.7 probes used per patient (EAC MTG8 Costing Update, 2021). Uncertainty regarding probe use (reduced from 50 to 25 uses) was addressed during sensitivity analysis in the costing update.
Overall post-operative morbidity	With TTFM: 6% Without TTFM: 16%	Becit *et al.* (2007): combination of re-exploration for bleeding, deep sternal infection, IABP insertion, peri- or post-operative infarction, overall mortality.	One conference abstract identified by the EAC (Laali *et al*. 2021) reported the following post-operative outcomes in 433 patients receiving TTFM to 492 patients not receiving TTFM but did not report the total number of patients experiencing at least one event (not mutually exclusive): major cardiac adverse event, peri-operative MI, post-operative cardiac arrest, need for ECMO, in-hospital overall mortality. Laali *et al.* 2021 did not report on re-exploration for bleeding, deep sternal infection or IABP insertion outcomes. The EAC have not identified any additional evidence to justify updating this parameter in economic modelling.

Variable	Value	Source	EAC comment
Overall post-operative mortality	With TTFM: 0% Without TTFM: 4%	Becit *et al.* (2007)	Only one conference abstract identified by the EAC (Laali *et al*. 2021) reported overall mortality, as 1.6% in patients receiving TTFM, and 3.3% in patients not receiving TTFM. In-hospital cardiac mortality was reported as 0.5% in patients receiving TTFM and 2.2% in those not. Reported values are in line with those included in the costing update (EAC MTG8 Costing Update, 2021), however the EAC notes that mortality does not influence costs in the updated economic model.
Re-exploration of bleeding	With TTFM: 3% Without TTFM: 3%	Becit *et al.* (2007)	The EAC have not identified any additional comparative evidence reporting on re-exploration of bleeding in patients receiving TTFM to those not; model parameter not updated.
Deep sternal infection	With TTFM: 1% Without TTFM: 1%	Becit *et al.* (2007)	The EAC have not identified any additional comparative evidence reporting deep sternal infection in patients receiving TTFM to those not; model parameter not updated.
IABP insertion	With TTFM: 1% Without TTFM: 7%	Becit *et al.* (2007)	The EAC have not identified any additional comparative evidence reporting IABP insertion in patients receiving TTFM to those not.
Peri- or postoperative myocardial infarction	With TTFM: 0% Without TTFM: 5%	Becit *et al.* (2007)	The EAC have not identified any additional comparative evidence reporting the occurrence of MI (combined peri- and post-operatively) in patients receiving TTFM to those not.
Hospital days to discharge	With TTFM: 8.2 Without TTFM: 8.3	Becit *et al.* (2007)	The EAC have not identified any additional comparative evidence reporting hospital day stays to discharge in patients receiving TTFM to those not.

Variable	Value	Source	EAC comment
Rate of patients with revisions	6.58%	Two studies contributed to mean revision rates: Becit *et al.* (2007): 9.0% Kieser *et al.* (2010): 4.2%	The EAC notes that the total revision rate used in the original Company economic model was on a per patient basis, however the type of revision (major or minor) was on a per graft basis. The EAC identified a total of 38 studies that reported the need for graft revision, 11 of which reported intra-operative revision occurring in between 0% and 11.6% of patients (Table 3). Within sensitivity analysis of the costing update the intra-operative revision rate was increased from 6.58% to 14.60% (EAC MTG8 Costing Update, 2021), which is greater than that reported in this updated evidence review. The EAC did not identiy any comparative evidence (comparing patients receiving TTFM to those not) to update the economic modelling.
Mean minor revision rate	34.7%	Two studies contributed to mean minor revision rates: Becit *et al.* (2007): 44.4% Kieser *et al.* (2010): 25.0%	The EAC did not identify any comparative evidence (comparing patients receiving TTFM to those not) which reported on minor or major revisions to update the economic modelling. Within sensitivity analysis of the costing update the minor revision rate was increased from 34.7% to 50% (EAC MTG8 Costing Update, 2021).
Duration of minor revision	2.5 minutes	Dr Kieser, e-mail correspondence	The EAC did not identify any additional evidence relating to this outcome.
Mean major revision rate	65.3%	Two studies contributed to mean major revision rates: Becit *et al.* (2007): 75.0% Kieser *et al.* (2010): 55.6%	The EAC did not identify any comparative evidence (comparing patients receiving TTFM to those not) which reported on minor or major revisions to update the economic modelling.

Variable	Value	Source	EAC comment
Duration of major revision (weighted mean of on-pump and off-pump)	42 mins	Dr Kieser, e-mail correspondence	The EAC did not identify any additional evidence relating to this outcome.
MACE	PI<5: 5.42% PI>5: 16.95%	Kieser *et al.* (2010)	Only one conference abstract identified by the EAC (Laali *et al*. 2021) reported MACE outcomes in patients receiving TTFM to those not, however did not report these by PI subgroups. The EAC have not identified any additional robust evidence to recommend updating this parameter in economic modelling. The EAC notes that altering this value within the updated economic model [model setting: Input data!D77] has no impact on costs.
Mortality	PI<5: 3.25% PI>5: 11.86%	Kieser *et al.* (2010)	Only one conference abstract identified by the EAC (Laali *et al*. 2021) reported mortality outcomes in patients receiving TTFM to those not, however did not report these by PI subgroups. The EAC have not identified any additional robust evidence to recommend updating this parameter in economic modelling. The EAC notes that altering this value within the updated economic model [model setting: Input data!D78] has no impact on costs.
Mortality, excluding emergency patients	PI<5: 2.00% PI>5: 9.26%	Kieser *et al.* (2010)	Only one conference abstract identified by the EAC (Laali *et al*. 2021) reported mortality outcomes in patients receiving TTFM to those not, however did not report these by emergency and non-emergency patient subgroups. The EAC have not identified any additional robust evidence to recommend updating this parameter in economic modelling. The EAC notes that altering this value within the updated economic model [model setting: Input data!D79] has no impact on costs.

Abbreviations: CI, confidence interval; EAC, external assessment centre; PSA, probabilistic sensitivity analysis; MACE, major adverse cardiovascular events; TTFM, transit-time flow measurement; PI, pulsatility index; IABP, intra-aortic balloon pump; SD, standard deviation

The EAC did not identify any randomised evidence comparing TTFM with no TTFM in patients undergoing CABG surgery. The most robust comparative evidence comes from one retrospective cohort study (Laali *et al.* 2021) that included 433 patients with TTFM and 492 patients without TTFM. This study was available in abstract form only, and reported limited in-hospital outcomes. Laali *et al.* (2021) reported that five patients in the TTFM group underwent revision (1.1%); however, the severity of revision is not reported. The EAC notes that a reduction in revision rate in the TTFM arm (from 6.58% in the base case economic model) would increase the cost savings associated with MiraQ. However, as Laali *et al.* (2021) did not report breakdown of in-hospital events as incorporated into the economic model (for example this study did not report re-exploration for bleeding, deep-sternal infection, intra-aortic balloon pump insertion and did not categorise revision as minor or major), the EAC would not consider it robust to make this univariate change to the economic model. The study reported no significant difference in peri-operative MI (0.5% with TTFM, 1% without TTFM, p=0.46), but with a significant difference in patients experiencing MACCE (2.1% with TTFM, 5.7% without TTFM, p<0.01), and post-operative cardiac arrest (0.7% with TTFM, 2.4% without TTFM, p=0.036) between the different arms of the study. However, as the study did not report the total number of patients experiencing either a peri- or post-operative myocardial infarction between arms (as incorporated in the economic model) and it is unclear from the study whether events are mutually exclusive, the EAC did not update the economic model using data from conference abstract for this individual outcome. The EAC notes that this study was also not prospectively powered to detect differences in these outcomes. The study also did not report on the other outcomes included in the economic model (CABG team composition, duration of TTFM, probes used per procedure, devices used per year), and did not subgroup outcomes by pulsatility index (PI less than 5, or greater than 5) in line with the current economic model structure. Therefore, the EAC did not change any of the values derived from the original comparative study by Becit *et al.* (2007) in the economic model.

The EAC notes that mortality and MACE inputs for patient subgroups (PI less than 5; PI greater than 5) within the economic model were derived from the cohort study by Kieser *et al.* (2010). The EAC have identified one comparative study (Laali *et al.* 2021) which reported MACE outcomes in 2.1% of patients receiving TTFM compared to 5.7% of patients not receiving TTFM. The EAC also identified three cohort studies (Jia *et al.* 2021; Su *et al.* 2018; Tang *et al.* 2021) which reported MACE outcomes in 2.0% to 14.9% of patients receiving TTFM. Due to the lack of robust evidence (with only one conference abstract and large heterogeneity across three identified single arm studies), the EAC did not further update rates of adverse events in the economic model.

The published evidence from a UK NHS setting is represented by a single centre with only one comparative study with a non-routinely used comparator; findings may not be easily generalisable across the wider NHS. The most robust comparative evidence (comparing patients receiving TTFM and those not) set in France was available in abstract form only, did not use randomization, and reported limited outcomes (Laali *et al.* 2021). Study design, outcome measures, follow-up lengths, comparators, TTFM cut-offs, and duration of follow-up data are heterogenous across the included 87 papers; therefore, the EAC concludes that the new evidence does not provide a strong case for updating the clinical parameters in the economic model.

3.7 Other relevant information

The EAC identified zero results for “MiraQ” or “VeriQ” in the FDA MAUDE database between 16/11/2011 and 31/01/2022. The EAC found one field safety notice for “MiraQ” on MHRA (search date: 03/02/2022), Table 7.

Table 7: Summary of Field Safety Notice

Date	Products	Serial numbers	Summary	Additional information
18/01/2018	VeriQ Systems VeriQ C Systems MiraQ Systems	All	Update to IFU (notice to provide supplementary information only)	Medistim is aware of incidence where flow measurement channels on Medistim systems have been operating with a significant zero-point offset value. The result is that flow measurements recorded with these channels will indicate too high or too low flow. Exploration of the issue have shown that this malfunction was caused by electrostatic discharge (ESD) damaging a component in the measurement chain on the Medistim systems, causing an offset from zero. Medistim test the ESD resistance during compliance testing to ensure we meet the requirements in the electromedical safety standard. However these events have shown that a severe ESD can surpass these requirements.

4. Conclusion

The EAC identified a total of 87 papers relevant to the decision problem. Despite the quantity of evidence reporting the use of Medistim TTFM devices, the EAC considers that there is insufficient new high quality comparative evidence (comparing outcomes with and without TTFM) to justify an update of the MTG8 guidance. Only one study compared TTFM with no TTFM in CABG patients, but it was was only available as a conference abstract, lacked a detailed description of methodology, and had limited reporting of in-hospital outcomes. Lack of comparative studies may be a consequence of ESC/EACTS Guidelines on myocardial revascularisation (2018) which report the benefit of TTFM in reducing adverse events and graft failure. The EAC notes that one of the Clinical experts stated that TTFM is used routinely for all CABG procedures within their centre, and therefore TTFM during CABG may represent standard of care in some hospitals. This is supported by the nine

new RCTs idenfitied in this evidence review, where TTFM was used in both arms. Therefore, it may be a challenge to develop further randomised evidence due to lack of clinical equipoise.

The EAC did identify one study, which compared patients with and without TTFM measurement and their one-year patency, and one- and five-year adverse event outcomes (Quin *et al.* 2021). The study was a subanalysis of the "Randomized On-Off Bypass (ROOBY)" trial, and included 1,067 patients with TTFM and 501 patients without TTFM measurements. However, this study was excluded due to the intervention being either the device by Medistim, or a competitor device by Transonic Systems. The intervention was at discretion of surgeon, and results were not reported for the different TTFM systems separately. No other randomised evidence was identified by the EAC which was powered to detect difference in TTFM in CABG patients.

The majority of evidence identified was single arm with large heterogeneity between studies in terms of patient and procedure characteristics (for example CAD severity, inclusion of concomitant procedures, different types and number of grafts, use of pump bypass, length of follow-up, imaging used for follow-up, definition of failure and criteria for revision). Due to this, the EAC did not update the adverse event parameters in the economic model.

The EAC also excluded 11 papers which discuss the use and clinical benefit of epicardial or high-frequency ultrasound functionality of the Medistim device when used alongside TTFM (Andreasen *et al.* 2020; Banjanovic *et al.* 2015; Di Giammarco *et al.* 2014; Di Giammarco *et al.* 2017b; Leviner *et al.* 2021; Iino *et al.* 2016; Kim *et al.* 2020a; Rosenfeld *et al.* 2021a; Rosenfeld *et al.* 2021b; Taggart *et al.* 2020; Wendt *et al.* 2019). This included two case reports that reported dissection (Banjanovic *et al.* 2015) with EUS despite normal flow measurements. Whilst out of scope for this review, this combination (TTFM and EUS) could be considered in separate guidance.

Appendix A – Relevant guidance

Published

NICE guidelines (clinical, public health, social care, medicine practice guidelines, safe staffing)

- Acute coronary syndromes (2020) NICE guideline NG185

All other NICE guidance and advice products

- QAngio XA 3D QFR and CAAS vFFR imaging software for assessing coronary stenosis during invasive coronary angiography (2021) NICE diagnostics guidance 43
- Rivaroxaban for preventing atherothrombotic events in people with coronary or peripheral artery disease (2019) NICE technology appraisal guidance 607
- DuraGraft for preserving vascular grafts (2019) NICE medtech innovation briefing 184
- Kendall DL for ECG monitoring in people having cardiac surgery (2019) NICE medtech innovation briefing 177
- HeartFlow FFRCT for estimating fractional flow reserve from coronary CT angiography (2017) NICE medical technologies guidance 607
- VEST external stent for coronary artery bypass grafts (2017) NICE medtech innovation briefing 115
- Somatom Definition Edge CT scanner for imaging coronary artery disease in adults in whom imaging is difficult (2016) NICE medtech innovation briefing 54 [updated 2017]
- Aquilion PRIME CT scanner for imaging coronary artery disease in adults in whom imaging is difficult (2016) NICE medtech innovation briefing 54 [updated 2017]
- New generation cardiac CT scanners (Aquilion ONE, Brilliance iCT, Discovery CT750 HD and Somatom Definition Flash) for cardiac imaging in people with suspected or known coronary artery disease in whom imaging is difficult with earlier generation CT scanners (2012) NICE diagnostics guidance 3 [updated 2017]
- Drug-eluting stents for the treatment of coronary artery disease (2008) NICE technology appraisal guidance 152 [updated 2020]

- Guidance on the use of coronary artery stents (2003) NICE technology appraisal guidance 71 [updated 2020]

NICE pathways

- Acute coronary syndromes: early management (2021) NICE pathway
- Acute coronary syndromes: secondary prevention and rehabilitation (2020) NICE pathway

Under development

NICE guidelines (clinical, public health, social care, medicine practice guidelines, safe staffing)

- No relevant results found

All other NICE guidance and advice products

- No relevant results found

Suspended or terminated

- No relevant results found

In topic selection

- No relevant results found

Appendix B – Literature search strategy

Adverse events sources	Date searched	Results and search terms
FDA medical devices MAUDE database	29/07/2021	No relevant results
MHRA - **Search for the indication. if you are getting no results for the device name**	29/07/2021	Medistim ASA: VeriQ, MiraQ [MHRA Reference: 2018/001/015/291/001]
Ongoing trials sources **Include completed trials that are within the date parameter specified by the analyst** Clinical trials.gov WHO International Clinical Trial Registry Platform (ICTRP) ISRCTN	29/07/2021	***Ongoing studies*** ACTRN12619000137190: Evaluation of coronary artery bypass grafts by intraoperative transit time flow measurement in three stages; on the resting heart, on beating heart, after heparin inactivation. Status: Recruiting Primary comparator: Standard CABG without routinely underwent TTFM Expected enrolment: 300 Estimated primary completion date:01/09/2025 Location: Russia ***Completed studies*** No relevant studies

Database searches:

Databases*	Date searched	No retrieved	Version/files
MEDLINE (Ovid)	30/07/2021	59	1946 to July 29, 2021
MEDLINE In-Process (Ovid)	30/07/2021	2	1946 to July 29, 2021
MEDLINE ePub ahead of print (Ovid)	30/07/2021	4	July 29, 2021
EMBASE (Ovid)	30/07/2021	80	1996 to 2021 July 29
CDSR (Wiley)	30/07/2021	0	Issue 7 of 12, July 2021
CENTRAL (Wiley)	30/07/2021	6	Issue 7 of 12, July 2021
HTA database (INAHTA)	02/08/2021	2	N/A
Econlit (Ovid - for economic searches)	30/07/2021	0	1886 to July 22, 2021
Total		153	
Total after de-duplication		95	

Search strategies

Database: Medline
Strategy used: 1 (VeriQ or MiraQ*).tw. (6) 2 Medistim.tw. (12) 3 or/1-2 (13)

4 (Transit* adj1 time* adj1 (flow* or measur*)).tw. (745)
5 (TTF or TTM or TTFM).tw. (4165)
6 ((Intra*operat* or funct*) adj3 graft* adj3 verifi*).tw. (16)
7 (("flow curve*" or "pulsatility index*" or "mean flow*") adj3 graft*).ti,ab. (52)
8 or/4-7 (4853)
9 Coronary Artery Bypass/ (50526)
10 (Coronary adj2 (arter* or vein*) adj2 (bypass* or surg* or revascular* or graft*)).tw. (42006)
11 CABG.tw. (16611)
12 or/9-11 (65869)
13 8 and 12 (232)
14 3 or 13 (237)
15 Animals/ not Humans/ (4833982)
16 14 not 15 (224)
17 limit 16 to ed=20160101-20211231 (66)
18 limit 17 to english language (59)

Database: MIP

Strategy used:

1 (VeriQ or MiraQ*).tw. (0)
2 Medistim.tw. (0)
3 or/1-2 (0)
4 (Transit* adj1 time* adj1 (flow* or measur*)).tw. (5)
5 (TTF or TTM or TTFM).tw. (139)
6 ((Intra*operat* or funct*) adj3 graft* adj3 verifi*).tw. (0)
7 (("flow curve*" or "pulsatility index*" or "mean flow*") adj3 graft*).ti,ab. (0)
8 or/4-7 (142)
9 Coronary Artery Bypass/ (0)

10 (Coronary adj2 (arter* or vein*) adj2 (bypass* or surg* or revascular* or graft*)).tw. (498)
11 CABG.tw. (258)
12 or/9-11 (544)
13 8 and 12 (2)
14 3 or 13 (2)
15 Animals/ not Humans/ (0)
16 14 not 15 (2)
17 limit 16 to dt=20160101-20211231 (2)
18 limit 17 to english language (2)

Database: MEP

Strategy used:

1 (VeriQ or MiraQ*).tw. (1)
2 Medistim.tw. (1)
3 or/1-2 (2)
4 (Transit* adj1 time* adj1 (flow* or measur*)).tw. (7)
5 (TTF or TTM or TTFM).tw. (120)
6 ((Intra*operat* or funct*) adj3 graft* adj3 verifi*).tw. (0)
7 (("flow curve*" or "pulsatility index*" or "mean flow*") adj3 graft*).ti,ab. (0)
8 or/4-7 (124)
9 Coronary Artery Bypass/ (0)
10 (Coronary adj2 (arter* or vein*) adj2 (bypass* or surg* or revascular* or graft*)).tw. (624)
11 CABG.tw. (335)
12 or/9-11 (691)
13 8 and 12 (4)
14 3 or 13 (6)
15 Animals/not Humans/(0)

16 14 not 15 (6)
17 limit 16 to dt=20160101-20211231 (5)
18 limit 17 to english language (4)

Database: Embase

Strategy used:

1 (VeriQ or MiraQ*).tw,dv. (39)
2 Medistim.tw,dm. (45)
3 or/1-2 (71)
4 (Transit* adj1 time* adj1 (flow* or measur*)).tw. (918)
5 (TTF or TTM or TTFM).tw. (9298)
6 ((Intra*operat* or funct*) adj3 graft* adj3 verifi*).tw. (35)
7 (("flow curve*" or "pulsatility index*" or "mean flow*") adj3 graft*).ti,ab. (68)
8 or/4-7 (10118)
9 coronary artery bypass graft/ (66211)
10 (Coronary adj2 (arter* or vein*) adj2 (bypass* or surg* or revascular* or graft*)).tw. (53557)
11 CABG.tw. (32688)
12 or/9-11 (90545)
13 8 and 12 (319)
14 3 or 13 (364)
15 nonhuman/ not human/ (3607776)
16 14 not 15 (349)
17 limit 16 to dc=20160101-20211231 (120)
18 limit 17 to english language (117)
19 limit 18 to (conference abstract or conference paper or "conference review") (37)
20 18 not 19 (80)

Database: CDSR & CENTRAL

Strategy used:

#1 (VeriQ or MiraQ*):ti,ab 2
#2 Medistim:ti,ab 8
#3 {or #1-#2} 8
#4 (Transit* NEAR/1 time* NEAR (flow* or measur*)):ti,ab 366
#5 (TTF or TTM or TTFM):ti,ab 1154
#6 ((Intra*operat* or funct*) NEAR/3 graft* NEAR/3 verifi*):ti,ab 0
#7 ((Flow* NEAR curve*) NEAR/3 graft*):ti,ab 1
#8 ((pulsatility NEAR index*) NEAR/3 graft*):ti,ab 4
#9 ((mean NEAR flow*) NEAR/3 graft*):ti,ab 22
#10 {or #4-#9} 1519
#11 MeSH descriptor: [Coronary Artery Bypass] this term only 5202
#12 (Coronary NEAR/2 (arter* or vein*) NEAR/2 (bypass* or surg* or revascular* or graft*)):ti,ab 10032
#13 CABG:ti,ab 5841
#14 {or #11-#13} 12745
#15 #10 and #14 44
#16 #3 or #15 49
#17 "conference":pt or (clinicaltrials or trialsearch):so 559928
#18 #16 not #17 with Cochrane Library publication date Between Jan 2016 and Jul 2021, in Cochrane Reviews 0
#19 #16 not #17 with Publication Year from 2016 to 2021, in Trials 6

Database: Econlit

Strategy used:

1 (VeriQ or MiraQ*).tw. (0)
2 Medistim.tw. (0)
3 or/1-2 (0)
4 (Transit* adj1 time* adj1 (flow* or measur*)).tw. (1)
5 (TTF or TTM or TTFM).tw. (27)
6 ((Intra*operat* or funct*) adj3 graft* adj3 verifi*).tw. (0)
7 (("flow curve*" or "pulsatility index*" or "mean flow*") adj3 graft*).ti,ab. (0)
8 or/4-7 (28)
9 [Coronary Artery Bypass/] (0)
10 (Coronary adj2 (arter* or vein*) adj2 (bypass* or surg* or revascular* or graft*)).tw. (56)
11 CABG.tw. (42)
12 or/9-11 (65)
13 8 and 12 (0)
14 3 or 13 (0)

Database: INAHTA

Strategy used:

16	((((CABG)) OR ((Coronary) AND (arter* OR vein*) AND (bypass* OR surg* OR revascular* OR graft*)) OR ("Coronary Artery Bypass"[mh])) AND ((((flow curve* OR pulsatility index* OR mean flow*) AND (graft*))) OR ((Intra*operat* OR funct*) AND (graft*) AND (Verifi*)) OR ((TTF OR TTM OR TTFM)) OR ((Transit*) AND (Time*) AND (Flow* OR measur*)))) OR ((Medistim*) OR ((VeriQ) OR (MiraQ*)))) FROM 2016 TO 2021	2
15	((((CABG)) OR ((Coronary) AND (arter* OR vein*) AND (bypass* OR surg* OR revascular* OR graft*)) OR ("Coronary Artery Bypass"[mh])) AND ((((flow curve* OR pulsatility index* OR mean flow*) AND (graft*))) OR ((Intra*operat* OR funct*) AND (graft*) AND (Verifi*)) OR ((TTF OR TTM OR TTFM)) OR ((Transit*) AND (Time*) AND (Flow* OR measur*)))) OR ((Medistim*) OR ((VeriQ) OR (MiraQ*)))	7
14	#13 OR #3	7
13	#12 AND #8	7
12	#11 OR #10 OR #9	155
11	(CABG)	57
10	(Coronary) AND (arter* OR vein*) AND (bypass* OR surg* OR revascular* OR graft*)	129
9	"Coronary Artery Bypass"[mh]	60
8	#7 OR #6 OR #5 OR #4	30
7	((flow curve* OR pulsatility index* OR mean flow*) AND (graft*))	24
6	(Intra*operat* OR funct*) AND (graft*) AND (Verifi*)	0
5	(TTF OR TTM OR TTFM)	1
4	(Transit*) AND (Time*) AND (Flow* OR measur*)	5
3	#2 OR #1	0
2	Medistim*	0
1	(VeriQ) OR (MiraQ*)	0

Notes:
Record any important decisions on how the strategy was developed The following changes were made to the 2016 strategy: • Added MiraQ* to line 1. Did not add truncation to VeriQ because there is a similar device that starts with this name and is unrelated. MiraQ is the new name of the device. • Added Measur* to line 4 and reduced truncation from 3 to 1, as it's a phrase and 3 was bring back noise • Added TTFM to line 5 • Added funct* to line 6 • Reduced lines 7-9 into line 7. Removed the abbreviation of PI and MF as it's a common measurement in cardiac surgery and was bringing back irrelevant results. Reduced three terms to phrase marks and included flow curve, which the device measures. Also included graft as the device is measuring the performance of those elements in the graft (hope that makes sense!). • Date limit – from 1st January 2016 to present. During peer review Lynda recommended changing lines 1 and 2 to all fields. This change (2 in Medline and 1 in Embase) was not applied after checking the additional records for relevancy. However, it could be considered for future updates. DARE and NHS EED were not searched as the date limit was from 2016 and both databases have not been updated since 2015.

Appendix C – Correspondence Log

Appendix C1: Communication with Company

#	Question	Answer
1.	Intervention: The EAC has identified studies which discuss TTFM during cardiac surgery but no device name or manufacturer have been listed. Are you aware of any other devices/manufacturers of TTFM, or can the EAC assume these studies refer to VeriQ/MiraQ exclusively?	There are two manufacturers of TTFM systems: Medistim and Transonic. Additional older versions of Medistim systems are Cardiomed and Butterfly. Most CABG papers include the name of the systems, but if this information is not included, we can not know for sure which system is used unless we know the centre. In the excel appendix 2 the studies can be sorted by vendor/model used.
2.	Comparator: The EAC has identified one study (Amin *et al.* 2018) which compares TTFM measured by VeriQC to free flow (after clipping and distal division of the LIMA, free blood flow measured in a cup in a fixed time period of 20 seconds). Is free flow considered standard of care of "clinical assessment of graft flow" in the UK NHS? [Is this comparator valid to final scope – page 5 of 7]	Measuring free flow is very rarely performed. It may be used as a comparator when investigating the accuracy of mean graft flow using TTFM.
3.	Comparator: The final scope (page 5 of 7) includes a list of 6 comparators to VeriQ/MiraQ. Can you identify which represent current NHS standard of care: • clinical assessment of graft flow • SPY indocyanine green fluorescence imaging • Electromagnetic flow meters • Intraoperative or completion Doppler (auscultation) • Intraoperative or completion Duplex imaging Intraoperative or completion angiogram	Intraoperatively, clinical assessment of graft flow is the most common method used in the UK, accounting for ~ 90% of all CABG cases. However, clinical assessment which effectively means external visual assessment and palpation of bypass grafts is notoriously unreliable. The former will only detect gross

		abnormalities and the latter can be completely misleading as even an occluded graft with thrombus can still transmit a pulse. According to Prof. Taggart from Oxford, none of the other methods mentioned are used in NHS today and very infrequently worldwide.
4.	Outcome: The final scope (page 5 of 7) also lists an outcome of interest as "long term morbidity and mortality". What time frame of "long-term" is of clinical interest: beyond 30 days, outcomes at 1 year or later?	The CABG operation is designed to last over 20-30y, and long-term outcome is influenced by a number of factors (patient characteristics, surgical technique, medication, comorbidities and so on). However, a surgical pre-requisite for good long-term graft patency and hence clinical outcome is a technically perfect anastomosis, and TTFM can help to ensure that this has been achieved before the patient leaves the operating room. A sub-optimal anastomosis with limited graft flow is associated with increased long-term mortality and morbidities.
5.	Population: The EAC has identified one study which included Patients undergoing CABG of the ascending descending artery in connection with a detected myocardial bridge. What proportion of patient undergoing CABG procedure have a myocardial bridge? (with such that, is this a common patient group treated in UK NHS?)	The number for UK is reported by Prof Taggart from Oxford to be significantly less than 5% of all coronary arteries. In a study from Japan in 2013, Hayakawa *et al.* calculated the frequency of coronary

		arteries embedded in myocardium, including myocardial bridges, to be 2.3% (7/299) of all coronaries (7.8% or 7/89 of all patients).
6.	Sub-population: No subgroups were listed within the final scope (page 5 of 7), however the EAC has identified a large number of cohort studies with a range of subgroup analyses: • on-pump and off-pump CABG (Amin *et al.* 2019) • SVG and arterial grafts (Amin *et al.* 2019), • stented and non-stented saphenous vein grafts, and arterial grafts (Amin *et al.* 2018a), • left and right coronary territory (Amin *et al.* 2018a), • diameter of target vessels, dichotomised as less than 1.5mm and greater or equal to 1.5 mm (An *et al.* 2019), • patients in whom ligation of the anterior descending artery was performed, and those not (Bazylev *et al.* 2018), • collateral filling from the contralateral vessel by the Rentrop grade (Gestrich *et al.* 2020), • grafting of the right internal mammary artery (RIMA) to bilateral or left target territories (Han *et al.* 2021), • meshed and unmeshed SVGs, • normal/abnormal TTFM results, and patent/failing angiography result at 12 months (Handa *et al.* 2016). Are all of these subgroup analyses relevant to the MTG8 guidance?	TTFM is relevant to use for intraoperative quality assessment in all patients, although as the EAC imply, the indications may be even stronger in some of these sub-groups.
7.	Are VeriQC and VeriQ considered equivalent in terms of TTFM measurement?	
8.	Please could you share your latest Instructions for Use for MiraQ	

9.	Please could you share your CE certification and Declaration of Conformity for MiraQ?	
10.	In the spreadsheet of published literature provided by Medistim the system used was stated as “Medistim and Transonic” for the Quin *et al.* 2020 study. Can you confirm that “transonic” is considered a comparator of MiraQ/VeriQ in terms of TTFM?	No, Transonic cannot be considered a comparator of VeriQ/MiraQ. The most frequently used TTFM parameters for intraoperative quality assessment are mean graft flow (MGF) and pulsatility index (PI). Transonic can be considered a comparator ONLY for MGF and not the other indices. The calculation of PI is dependent on the filter setting of the system and the default for this is different for Transonic and VeriQ/MiraQ. Consequently, regarding PI, Transonic cannot be considered a comparator.
11.	Can you clarify if a literature search was used to create the list of 161 papers in the spreadsheet that Medistim provided to NICE?	The list is based on continuous monitoring of new publications using relevant search terms in Google Scholar and PubMed. The list is updated after the yearly clinical evaluation update required for class III medical devices. A very recent article on TTFM written by 19 of the worlds most renowned cardiac surgeons was published in Circulation in October 2021, after the previous publication list was issued. This publication is attached to this document [Gaudino *et al.* 2021]

12.	Is CardioMed an earlier version of VeriQ/MiraQ? Does it have TTFM functionality?	Yes, and it had TTFM functionality similar to Veri Q/MiraQ. Cardiomed was launched in 1994 and was discontinued in 1997 when Butterfly was launched.
13.	Is Butterfly an earlier version of VeriQ/MiraQ? Does it have TTFM functionality?	Yes, and it had TTFM functionality similar to Veri Q/MiraQ. Butterfly was launched in 1997 and was discontinued in 2004 when VeriQ was launched.
14.	Are QuickFit probes used with VeriQ/MiraQ? Does a user need a QuickFit probes to conduct TTFM or are other probes compatible?	Yes, QuickFit probes are used with both VeriQ and MiraQ. All TTFM probes, including QuickFit probes, can be used with VeriQ and MiraQ. All Medistim TTFM probes have similar functionality but differs in some design features.
15.	Can you clarify the differences between SonoQ and VeriQ/MiraQ? Does it have TTFM functionality?	SonoQ has TTFM functionality similar to VeriQ/MiraQ. However, the TTFM probes are not interchangeable between the SonoQ and VeriQ/MiraQ. SonoQ was discontinued in 2021.
16.	Are VeriQC and VeriQ considered equivalent in terms of TTFM measurement?	Yes. The only difference between VeriQ and VeriQC is that VeriQC has additional imaging capabilities if connected to a Medistim imaging probe.
17.	Please could you share your latest Instructions for Use for MiraQ?	See attachment
18.	Please could you share your CE certification and Declaration of Conformity for MiraQ?	See attachment

Appendix C2: Communication with Clinical experts

#	Question	Answer
1.	Intervention: The EAC has identified studies which discuss TTFM during cardiac surgery but no device name or manufacturer have been listed. Are you aware of any other devices/manufacturers of TTFM, or can the EAC assume these studies refer to VeriQ/MiraQ exclusively?	Expert 1: I am unaware of any other TTFM devices other than VeriQ/MiraQ from Medistim Expert 2:
2.	Comparator: The EAC has identified one study (Amin *et al.* 2018) which compares TTFM measured by VeriQC to free flow (after clipping and distal division of the LIMA, free blood flow measured in a cup in a fixed time period of 20 seconds). Is free flow considered standard of care of "clinical assessment of graft flow" in the UK NHS? [Is this comparator valid to final scope – page 5 of 7]	Expert 1: Qualitative free flow is the standard of care for the clinical assessment of IMA flow; few centres use quantitative free flow as described by Amin *et al.* Expert 2:
3.	Comparator: The final scope (page 5 of 7) includes a list of 6 comparators to VeriQ/MiraQ. Can you identify which represent current NHS standard of care: • clinical assessment of graft flow • SPY indocyanine green fluorescence imaging • Electromagnetic flow meters • Intraoperative or completion Doppler (auscultation) • Intraoperative or completion Duplex imaging • Intraoperative or completion angiogram	Expert 1: Clinical assessment of graft flow is the only current standard of care: • Qualitative free IMA flow • Hand injection of heparinised blood down a vein or radial graft after the distal anastomosis (qualitative) • Cardioplegia infusion rate down a vein or radial graft after the distal anastomosis (quantitative) • Pulsatility or compressibility of the completed graft Expert 2:
4.	Outcome: The final scope (page 5 of 7) also lists an outcome of interest as "long term morbidity and mortality". What time frame of "long-term" is of clinical interest: beyond 30 days, outcomes at 1 year or later?	Expert 1: 'Long-term' should be at least 1 year, but ideally 3-5 years, when CABG outcomes diverge from multi-vessel PCI

#	Question	Answer
		Expert 2:
5.	Population: The EAC has identified one study which included Patients undergoing CABG of the ascending descending artery in connection with a detected myocardial bridge. What proportion of patient undergoing CABG procedure have a myocardial bridge? (such as, is this a common patient group treated in UK NHS?)	Expert 1: Myocardial bridging is a rare indication for CABG; this is not a common patient group. Expert 2:
6.	Sub-population: No subgroups were listed within the final scope (page 5 of 7), however the EAC has identified a large number of cohort studies with a range of subgroup analyses: • on-pump and off-pump CABG (Amin *et al.* 2019), • SVG and arterial grafts (Amin *et al.* 2019), • stented and non-stented saphenous vein grafts, and arterial grafts (Amin *et al.* 2018a), • left and right coronary territory (Amin *et al.* 2018a), • diameter of target vessels, dichotomised as less than 1.5mm and greater or equal to 1.5 mm (An *et al.* 2019), • patients in whom ligation of the anterior descending artery was performed, and those not (Bazylev *et al.* 2018), • collateral filling from the contralateral vessel by the Rentrop grade (Gestrich *et al.* 2020), • grafting of the right internal mammary artery (RIMA) to bilateral or left target territories (Han *et al.* 2021), • meshed and unmeshed SVGs, • normal/abnormal TTFM results, and patent/failing angiography result at 12 months (Handa *et al.* 2016). Are all of these subgroup analyses relevant to the MTG8 guidance?	Expert 1: Any recommendation should apply to all CABG procedures, but these subgroups may be of particular relevance: • on-pump and off-pump CABG • vein and arterial grafts Expert 2:

Appendix D – Additional evidence

Appendix D1 – Excluded studies (from NICE literature search)

	Author (year)	Reason for exclusion
1.	Amin *et al.* 2018c	Outcomes: compares TTFM between left and right territories, and conducted multivariate analysis, but does not report on any outcomes of final scope.
2.	Andreasen *et al.* 2020	Main intervention of interest was intraoperative EUS using a stabilising device (EndoClip); TTFM was performed at different time points during surgery at surgeon's discretion in addition to EUS.
3.	Banjanovic *et al.* 2015	Intervention: EUS using VeriQC reported but TTFM normal Study design: series of case reports
4.	Bazylev *et al.* 2020	Cohort (retrospective), subgroup analysis depending on type of bypass grafting of PIVA, however does not report on outcomes included in scope
5.	Beketaev *et al.* 2015	Study design: letter to editor (original paper included in previous guidance review)
6.	Bozinovski *et al.* 2020	Study design: commentary, primary evidence already included in sift 1 reference list.
7.	Di Giammarco *et al.* 2017a	Study design: systematic review, Intervention: TTFM (VeriQ, MiraQ, Medistim not explicitly mentioned), inclusion of EUS (not in scope); - D'Ancona *et al.* 1999 excluded* - Takami *et al.* 2001 excluded* - Di Giammorco *et al.* 2006 excluded* - Kim *et al.* 2005 excluded* - Becit *et al.* 2007 excluded* - Tokuda *et al.* 2007 excluded* - Kieser *et al.* 2010 excluded* - Jokinen *et al.* 2011 excluded* - Walker *et al.* 2013 excluded† - Quin *et al.* 2014 excluded (used Transonic Systems, Inc, or Medtronic, Inc TTFM devices, not MiraQ or VeriQ) - Schmitz *et al.* 2003 excluded* - Leong *et al.* 2005 excluded* - Hassanein *et al.* 2005 excluded* - Canver *et al.* 1992 excluded* - Onorati *et al.* 2007 excluded* - Kim *et al.* 2011 excluded* - Lehnert *et al.* 2015 excluded† - Acipayam *et al.* 2015 included - Honda *et al.* 2015 included - Di Giammarco *et al.* 2014 excluded (Intervention TTFM and EUS, TTFM measured after EUS in off-pump cases, comparator is need for surgical revision which was guided by TTFM and EUS. Change in diagnostic accuracy with and without EUS reported)
8.	Di Giammarco *et al.* 2017b	Intervention: focus on EUS (not in scope) normal TTFM Study design: series of case reports
9.	Hashim *et al.* 2019	Study design: letter to editor (original paper included in updated literature search)

	Author (year)	Reason for exclusion
10.	Jia *et al.* 2021	Intervention: intraoperative TTFM (device not reported, corresponding author contacted, no response by 10/03/2022), fast Fourier transform (FFT) processing of the TTFM waveforms.
11.	Kassimis *et al.* 2017	Study design: case report (n=1)
12.	Kieser *et al.* 2018	Study design: review - Bauer *et al.* 2005 excluded* - Becit *et al.* 2007 excluded* - Herman *et al.* 2008 excluded* - Kieser *et al.* 2010 excluded*
13.	Kim *et al.* 2015	Population: radiocephalic arteriovenous fistula (AVF)
14.	Krasopoulos *et al.* 2020	Outcome: reports predictors of flow only (no additional outcomes from scope reported)
15.	Leviner *et al.* 2021	Intervention: reports use of HFUS (EUS) and TTFM guiding decision making (HFUS out of scope) Outcomes: comparison of flow measurements pre- and post-protamine.
16.	Li *et al.* 2019	Intervention: intraoperative TTFM (device not reported, corresponding author contacted, no response as of 10/03/2022
17.	Mao *et al.* 2020	Intervention: TTFM (device not reported, corresponding author contacted, no response as of 10/03/2022)
18.	Mootoosamy *et al.* 2016	Study design: case report
19.	Niclauss *et al.* 2017	Study design: review: - Honda *et al.* 2015 included - Lehnert *et al.* 2015 excluded† - Handa *et al.* 2015 excluded (work in progress report, superseded by Handa *et al.* 2016) - Uehara *et al.* 2015 included - Walker *et al.* 2013 excluded† - Bigdeli *et al.* 2011 excluded* - Jokinen *et al.* 2011 excluded* - Gao *et al.* 2010 excluded* - Singh *et al.* 2010 excluded* - Une *et al.* 2013 included
20.	Niclauss *et al.* 2018	Study design: case report Intervention: TTFM device not named
21.	Noda *et al.* 2021	Intervention: TTFM device not named (corresponding author contacted, no response as of 10/03/2022)
22.	Ohmes *et al.* 2017	Study design: review - Di Giammarco *et al.* 2006 excluded* - Takami *et al.* 2006 excluded* - Hatada *et al.* 2011 excluded* - Amin *et al.* 2016 excluded (Study design: review) - Kieser *et al.* 2010 excluded* - Tokuda *et al.* 2008 excluded* - Kim *et al.* 2005 excluded* - Di Giammarco *et al.* 2014 excluded (Intervention TTFM and EUS, TTFM measured after EUS in off-pump cases, comparator is need for surgical revision which was guided by TTFM and EUS. Change in diagnostic accuracy with and without EUS reported) - Leacche *et al.* 2009 excluded* - Desai *et al.* 2006 excluded* - Balacumaraswami *et al.* 2005 excluded*

	Author (year)	Reason for exclusion
23.	Piciche *et al.* 2019	Study design: letter to editor (original article Hashim *et al.* 2018 included)
24.	Quin *et al.* 2021	Intervention: examines TTFM use in ROOBY trial (Quin *et al.* 2014: excluded as included Transonic or Medtronic) and compared angiographic and clinical outcomes against patients whose grafts were not assessed with TTFM.
25.	Rosenfeld *et al.* 2021b	Intervention: Reports use of HFUS and TTFM guiding decision making (HFUS out of scope)
26.	Silva *et al.* 2020	Study design: systematic review and meta-analysis (N=25) - Amin *et al.* 2019 included - Balacumaraswami *et al.* 2008 excluded* - Boodhwani *et al.* 2006 excluded* - Cerqueira *et al.* 2012 included - Cetin *et al.* 2006 excluded* - D'Ancona *et al.* 2000 excluded* - Hassanein *et al.* 2005 excluded* - Hirotani *et al.* 2001 excluded* - Kieser *et al.* 2010 excluded* - Kjaergard *et al.* 2004 excluded* - Leong *et al.* 2005 excluded* - Nakajima *et al.* 2019 included - Reineke *et al.* 2012 included - Sanisoglu *et al.* 2003 excluded* - Santarpino *et al.* 2009 excluded* - Schmitz *et al.* 2003 excluded* - Seetharama Bhat *et al.* 2019 included - Takami and Ina 2002 excluded* - Walpoth *et al.* 2008 excluded* - Mannacio *et al.* 2011 excluded* - Walpoth *et al.* 1996 excluded*
27.	Taggart *et al.* 2020	Intervention: Reports use of HFUS and TTFM guiding decision making (HFUS out of scope)
28.	Takami *et al.* 2018	Study design: review
29.	Thuijs *et al.* 2019	Study design: systematic review and meta-analysis (N=35): - Hashim *et al.* 2017 included - Hiraoka *et al.* 2017 included - De Leon *et al.* 2017 included (De Leon *et al.* 2020) - Handa *et al.* 2016 included - Oshima *et al.* 2016 included - Honda *et al.* 2015 included - Di Giammarco *et al.* 2014 excluded (Intervention TTFM and EUS, TTFM measured after EUS in off-pump cases, comparator is need for surgical revision which was guided by TTFM and EUS. Change in diagnostic accuracy with and without EUS reported) - Quin *et al.* 2014 (used Transonic Systems, Inc, or Medtronic, Inc TTFM devices, not MiraQ/VeriQ) - Harahsheh *et al.* 2012 included - Kuroyanagi *et al.* 2012 included - Kieser *et al.* 2010 excluded* - Handa *et al.* 2009 excluded* - Nordgaard *et al.* 2009 excluded*

	Author (year)	Reason for exclusion
		- Santarpino *et al.* 2009 excluded* - Waseda *et al.* 2009 excluded* - Herman *et al.* 2008 excluded* - Onorati *et al.* 2008 excluded* - Becit *et al.* 2007 excluded* - Mujanovic *et al.* 2007 excluded* - Onorati *et al.* 2007 excluded* - Desai *et al.* 2006 excluded* - Poston *et al.* 2006 excluded* - Balacumaraswami *et al.* 2005 excluded* - Kim *et al.* 2005 excluded* - Leong *et al.* 2005 excluded* - Onorati *et al.* 2005 excluded* - Bergsland *et al.* 2004 excluded* - Gwozdziewicz *et al.* 2004 excluded* - Guden *et al.* 2003 excluded* - Sanisoglu *et al.* 2003 excluded* - Groom *et al.* 2001 excluded* - D'Ancona *et al.* 2000 excluded* - Jakobsen & Kjaergard *et al.* 1999 excluded* - Walpoth *et al.* 1998 excluded* - Canver and Dame 1994 excluded*
30.	Uehara *et al.* 2015	Intervention: power spectral analysis of TTFM waveform (MemCalc software)
31.	Urso *et al.* 2017	Full text available only in non-English language, intervention: no confirmation of VeriQ or MiraQ device used.
32.	Wendt *et al.* 2019	Intervention: HFUS used before TTFM (HFUS used to evaluate LIMA graft after harvesting but before clipping, evaluate the aortic clamping and cannulation site, and when on-pump, the targets vessels were scanned by HFUS). Unable to unpick outcome related to HFUS or TTFM intervention.
33.	Zhao *et al.* 2013	Intervention: Transonic device
*assumed considered within the original assessment report (2011) †included within the NICE evidence review (2016)		

Appendix D2 – Excluded studies (from Company literature search not identified in NICE literature search)

#	Author	Year	Reason for exclusion
1.	Abdalghafoor	2021	Study design: case series (n=2)
2.	Ahmed	2019	Study design: case report (n=1)
3.	Akhrass	2021	Study design: review of techniques
4.	Akhrass	2021	Study design: editorial; Intervention: no mention of TTFM/MiraQ/VeriQ/Medistim
5.	Akiyoshi	2020	Study design: case report (n=1)
6.	Andreasen	2019	Study design: case report (n=1); Intervention: TTFM in combination with EUS and EchoClip
7.	Balkhy	2020	Intervention: Robotic beating heart totally endoscopic coronary artery bypass (TECAB)
8.	Balkhy	2022	Intervention: Robotic beating heart totally endoscopic coronary artery bypass (TECAB)
9.	Barca	2019	Study design - case report (n=1)
10.	Basman	2020	Population: Patients undergoing hybrid coronary revascularisation (HCR) as an alternative to CABG and PCI.
11.	Bazylev	2016	Language: Non-English
12.	Bazylev	2018	Intervention: comparison of transthoracic ultrasound duplex scanning and intraoperative doppler flowmetry
13.	Benetti	2017	Duplicate: results already included in Benetti *et al.* 2021
14.	Brereton	2018	Study design: description of technique
15.	Brozzi	2019	Study design: case report (n=1), patient received a combination of CABG and liver transplant
16.	Chen	2019	Study design: CABG tips for young surgeons
17.	Chia	2021	Study design: Case report (n=1)
18.	Di Giammarco	2018	Study design: Review of studies looking at methods of graft assessment - Kim *et al.* 2005 excluded* - Di Giammarco *et al.* 2006 excluded* - Tokuda *et al.* 2007 excluded* - Kieser *et al.* 2010 excluded*
19.	Dimon	2021	Study design: Editorial
20.	Droc / Wendt	2016	Study design: Textbook chapter describing surgical technique Intervention: Medistim only specifically mentioned for ECUS (not TTFM)
21.	Emerson	2016	Study design: Review: description of CABG techniques
22.	Fukui	2016	Study design: Review (no specific reference to check for TTFM/MiraQ/VeriQ/Medistim)

#	Author	Year	Reason for exclusion
23.	Gaudino in collaboration with the Coronary Task Force of EACTS	2020	Study design: Review/guidelines Intervention: Mention of TTFM but not specifically Medistim/VeriQ/MiraQ - Silva *et al.* 2020 excluded (systematic review and meta-analysis) - Thuijs *et al.* 2019 excluded (systematic review and meta-analysis) - Taggart *et al.* 2020 excluded (HFUS and TTFM guiding decision making not reported exclusively) - Niclauss *et al.* 2017 excluded (review)
24.	Giambruno	2018	Intervention: robotic-assisted direct CABG
25.	Gradinariu	2021	Study design: Review - Gaudino *et al.* 2020 excluded (review) - Thuijs *et al.* 2019 excluded (systematic review and meta-analysis) Note: Mentions lack of randomised evidence of TTFM vs no TTFM
26.	Hanafy	2021	Population: excluded patients with mean graft flow <10 ml/s or PI > 5. Note that the number of patients excluded due to this reason was not reported.
27.	Hayashi	2017	Intervention: mixed intervention, TTFM (Medistim) only routinely used from 2002 (recruitment period 2000 to 2014). Outcomes: Mortality, graft failure outcomes not reported exclusively in those with and without TTFM.
28.	Hemli	2020	Study design: Textbook chapter describing robotic surgical techniques
29.	Hirakoa	2017	Included (also identified from references of systematic review)
30.	Iino	2016	Study design: Case report (n=1) Rare adverse event (air lock in a RITA graft), discovered by EUS.
31.	Ishida	2021	Intervention: does not included TTFM
32.	Kieser	2017	Study design: Review (not systematic, no search reported)
33.	Kieser	2018	Study design: Review
34.	Kim	2020b	Intervention: TTFM and EUS conducted immediately after anastomosis, action of clinician guided by EUS (Note: device for TTFM not explicitly stated, but VeriQ explicitly stated for EUS).
35.	Kinoshita and Asai	2016	Study design: Textbook chapter - [meta analysis] Balacumaraswami *et al.* 2007 excluded* - Kim *et al.* 2005 excluded* - Di Giammarco *et al.* 2006 excluded* - Tokuda *et al.* 2007 excluded*

#	Author	Year	Reason for exclusion
36.	Lee	2019	Duplicate: preprint of Lee *et al.* 2020 included (same KCT0002047 trial number)
37.	Magarakis	2021	Study design: case report (N=1)
38.	Marin-Cuartas	2021	Study design: Review of different methods of graft flow assessment (not systematic)
39.	Maskell	2021	Study design: Literature review (search reported) of papers comparing semi-skeletonised with pedicled harvesting of LIMA - Wimmer-Greinecker *et al.* 1999 excluded* - Lorberboym *et al.* 2001 excluded* - Ozulku and Aygun 2016 excluded (Intervention: no mention of TTFM measurements) - Satdhabudha and Noppawinyoowong 2017 included - Abdurrahman Kara 2018 excluded (Intervention: no mention of TTFM measurements)
40.	Miao	2017	Outcomes: subgroup analysis of patients undergoing off-pump CABG with emergency conversion to on-pump CABG, and statistical comparison of those who died and those who survived. TTFM routinely used in all procedures, however TTFM outcomes not reported.
41.	Mohsin	2021	Duplicate: pre-proof of Mohsin *et al.* 2021 (below)
42.	Mohsin	2021	Intervention: No mention of TTFM used in patients. Study design: Case reports (n=2).
43.	Nagendran	2018	Intervention: Robotic assisted surgery
44.	Nakajima	2019	I Included (also identified from references of systematic review)
45.	Neumann	2018	Study design: ESC Guidelines - Kieser *et al.* 2010 excluded* - Mujanovic *et al.* 2007 excluded* - Jokinen *et al.* 2011 excluded* - Lehnert *et al.* 2015 excluded† - Niclauss *et al.* 2017 excluded (Study design: review)
46.	Nisivaco	2017	Study design: Case report (n=1) Intervention: redo robotic endoscopic beating heart coronary bypass (TECAB) after previous TECAB
47.	Padmanabhan	2021	Study design: Editorial Intervention: focus on intraoperative TEE

#	Author	Year	Reason for exclusion
48.	Ramponi	2018	Study design: Description of surgical techniques/approaches - Amin *et al.* 2016 excluded (Study design: review)
49.	Rosseikin	2019	Language: Russian Intervention: no mention of TTFM in abstract
50.	Seco	2021	Study design: Description of technique - Brereton *et al.* 2018 excluded (Study design: description of technique) - Neumann *et al.* 2019 excluded (Study design: guidelines) - Amin *et al.* 2016 excluded (Study design: review)
51.	Semchenko	2020	Intervention: All grafts were patent according to intraoperative blood flow assessment by ICG angiography with SPY imaging system (Novadaq) and/or TTFM Medistim (results not exclusive to Medistim device, and not reported separately)
52.	Shahinian	2017	Study design: Case report (n=1). Patient underwent emergent CABG surgery after receiving out-of-hospital resuscitation as a result of MI using LUCAS CPR system. TTFM (Medistim) was used to measure graft flow.
53.	Shehada	2020	Study design: Conference abstract only (oral presentation). Note focused on coronary endarterectomy within CABG (severe and diffuse CAD)
54.	Sigaev	2021	Intervention: Combined use of TTFM and ECUS. Language: Russian (full paper not available in English)
55.	Small	2021	Study design: Review (not reporting of systematic search) - Kieser *et al.* 2010 excluded* - Sousa-Uva *et al.* 2018 excluded (Study design: review guidelines) - Sakabe *et al.* 2020 included - Chin *et al.* 2003 excluded*
56.	Taggart	2021	Intervention: TTFM not measured in all patients (“when available”).
57.	Tolegenuly	2021	Study design: Doctoral thesis
58.	Torregrossa	2016	Study design: Case report (n=1) describing technique for hybrid robotic CABG
59.	Trachiotis	2021	Study design: Editorial
60.	Vaporciyan	2017	Study design: Delphi approach to developing a checklist to assess construction of a coronary artery bypass.

#	Author	Year	Reason for exclusion
61.	Vigano	2019	Study design: Case report (n=1) on adverse event during CABG (air embolism in SVG) detected by TTFM (VeriQ)
62.	Villaescusa	2018	Language: non-English (Spanish)
63.	Vondran	2021	Study design: invited commentary Intervention: HFUS/TTFM
64.	Xenogiannis	2021	Study design: Review (no systematic search)
65.	Yanagawa / Puskas	2016	Study design: Review (description of OPCAB technique)
66.	Zhang	2019	Outcomes: effects of isoflurane preconditioning on MiRs and mRNAs levels in the LIMA graft with propofol in patients undergoing off-pump coronary artery bypass grafts. No long-term follow-up. No reporting of results from TTFM.
67.	Zientara	2019	Intervention: TTFM device not named (corresponding author contacted, no response as of 10/03/2022)
*assumed considered within the original assessment report (2011) †included within the NICE evidence review 2016			

Appendix D3 – Study characteristics of included clinical evidence

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
1.	Acipayam *et al.* 2015 Turkey	Cohort – retrospective (n=60) Intervention: VQ-1101 (Medistim) intraoperatively; EAC assumes this is VeriQ	Patients undergoing isolated CABG. Patients where a sequential or Y-graft were used were included in analysis (n=80). Authors state that "During the TTFM, we preferred to keep cardiac orientation stable so 60 patients were selected for the study from this group"; unclear on selection criteria. All CABG performed under cardiopulmonary bypass, at mild body hypothermia and on arrested heart by the same surgical team. Recruitment period between February 2010 and December 2011. Exclusion criteria: any other cardiovascular surgical intervention. No. of centres: single centre	Graft revision, flow measurements between graft techniques, mortality (30 days), acute MI, angina (30 days).	
2.	Amin *et al.* 2018a UK	Subgroup from RCT (n=35, 115 grafts) Intervention: VeriQC (Medistim). Each patient received 1 external stent (VEST) to a single SVG, randomly assigned intraoperatively to either the right or left coronary territory. One	Patients scheduled for on-pump multi-vessel CABG including the LIMA to the LAD artery and SVG to both the right and left coronary territories, target vessel diameter 1.5mm or greater, with coronary artery stenosis of great than 75% and with an adequately dimensioned distal vascular bed as assessed by preoperative angiography. Recruitment between October 2015 and January 2017. Exclusion criteria: patients with only left-sided or only right-sided coronary disease.	Need for graft revision.	Likely overlap with Amin *et al.* 2019; however unconfirmed

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
		or more SVGs remained non-stented and served as control.	No. of centres: single centre		
3.	Amin *et al.* 2018b UK	Cohort (n=60) Intervention: VeriQC (Medistim) Comparator: free flow (after clipping and distal division of the LIMA, free blood flow measured in a cup in a fixed time period of 20 seconds)	Consecutive patients undergoing elective myocardial revascularisation, using LIMA as 1 of the conduits. Recruitment between November 2015 and April 2016. Exclusion criteria: patients with extensively diseased LIMA, with obvious sign of haematoma, or damaged in any way that could potentially adversely affect flow. No. of centres: single centre	Accuracy and precision of TTFM in an arterial graft when compared with free flow.	Double blood flow measurement: during rest and after vasodilation. Intervention and comparator measurements taken simultaneously.
4.	Amin *et al.* 2019 UK	Cohort (n=268, 506 grafts to the left territory of which 336 were arterial grafts and 170 SVG) Intervention: VeriQC (Medistim) Comparator: N/A	Patients undergoing elective or urgent on-pump or off-pump CABG between July 2015 and April 2017, where TTFM was routinely performed. Exclusion criteria: graft anastomosed to the right coronary territory No. of centres: single centre	Need for graft revision (grafts were revised if mean graft flow was <20 ml/min or PI was >5 with obvious or detectable issues either by visual inspection or by high-frequency ultrasound imaging of the anastomosis)	Comparison of on-pump and off-pump subgroups, and SVG and arterial graft subgroups. Only post-revision TTFM measurements were included in the analysis.

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
5.	An *et al.* 2019 ŧChina	Cohort (n=212) Intervention: VeriQ (Medistim), and CT angiography at 1 year. Comparator: N/A	Patients undergoing isolated CABG (on- or off-pump), receiving aortosequential SVG to non-left anterior descending targets and the LIMA to the LAD coronary artery. Recruitment between January 2013 and December 2016. Exclusion criteria: patients without computed tomography angiography at one year follow-up. No. of centres: single centre	Graft patency evaluated using CT angiography at 1 year follow-up, failure defined as non-visualisation or poor stringy visibility of the graft. In sequential SVGs, each anastomotic segment was regarded as a separate bypass graft.	CT angiography conducted at 1 year to review graft patency.
6.	Bazylev *et al.* 2018 ŧ Russia	Cohort (n=17) Intervention: VeriQ (Medistim) intraoperatively, and coronary angiography at follow-up over three years Comparator: N/A	Patients undergoing CABG of the ADA in connection with a detected myocardial bridge. In all patients the surgical approach was via median sternotomy, with assisted circulation, and LITA used as a conduit. Recruitment period not defined. Exclusion criteria: Not reported. No. of centres: single centre	Blood flow in graft before removal of clamp from aorta, blood flow after clamp removed, graft occlusion/patency.	Coronary angiography conducted during follow-up (up to 72 months), however it is not clear whether all patients were reviewed at the same time points, or reviewed multiple times (follow-up poorly reported). Subgroup analysis conducted: patients in whom the anterior descending aorta

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
					was ligated and those not.
7.	Benetti *et al.* 2021 Argentina	Cohort – retrospective (n=70) Intervention: Medistim device Comparator: N/A	Patients operated upon with mini off-pump CABG, through sternotomy, with LITA to LAD bypass over 20 years (years not defined), included some patients with hybrid revascularisation. Exclusion criteria: not reported No. of centres: single centre	Operative mortality, intraoperative revision, long-term patency, mortality at follow-up	
8.	Borowski *et al.* 2017 Germany	Cohort – retrospective (n=69) Intervention: VeriQ (Medistim) Comparator: coronary angiography (CTO estimated over 3 months pre-operatively; catheterisation data also collected at post-discharge follow-up, when applicable)	Patients with coronary heart disease undergoing elective CABG, including single graft to chronic totally occluded RCA (defined as complete interruption of blood flow assessed by coronary angiography, with duration of at least 3 months estimated from patient records). All patients operated on using on-pump technique. Recruitment period between 2010 and 2015. Exclusion criteria: patients with left coronary dominance, concomitant valve disease, CTO-RCA bypassed via sequential graft, patients with repeat revascularisation, patients with intraoperative graft failure due to poor quality of DAS or abnormal signal pattern on TTFM.	Correlation between maximal diameter of recipient artery and flow, outcomes from follow-up (death, stroke, bleeding, infarction, cardiac catheterisation).	Univariate analysis to determine if flow or diameter were different between various patient subgroups.

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
			No. of centres: single centre~~l~~		
9.	Cerqueira Neto *et al.* 2012 Brazil	Cohort – retrospective (n=35) Intervention: Medistim (transducers and BF 2004 display); EAC assumes Butterfly device. Comparator: N/A	Consecutive patients with CAD undergoing CABG, either on- or off-pump. All patients underwent CABG through median sternotomy. Recruitment period between March 2010 and September 2010. Exclusion criteria: patients undergoing previous heart surgery that required associated intraoperative procedures, emergency surgery or those who required use of IABP. No. of centres: single centre	Short term mortality, MI, need for PCI (within 30 days), revision	Subgroup analysis of off-pump and on-pump. Intervention sterilised with ethylene oxide (and may include EUS).
10.	Chang *et al.* 2018 Korea Lower versus Upper left saphenous vein composite graft based on the LITA for coronary artery bypass grafting (LUMEN) trial [NCT01974492]	RCT (n=26) 1:1 randomisation to surgical strategy on the basis of side-arm conduit used to construct Y-composite graft. Intervention (n=13): graft using upper leg vein Comparator (n=13): graft using lower leg vein	Patients aged 40 to 75 years, first-time isolated CABG for multi-vessel CAD on non-emergency basis, expected to received a Y-composite graft based on the in situ LITA for complete revascularisation. All procedures conducted off-pump. Recruitment period between November 2013 and February 2014. Exclusion criteria: unavailable SV, history of previous cardiac surgery, medical history that might limit the possibility of mid-term follow-up such as malignant disease, estimated LVEF ≤25%.	Graft patency	Subgroup analysis by LLV and ULV:MF, patency at 1 year follow-up.

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
		All patients underwent intraoperative TTFM assessment (Medistim; device not reported) before sternal closure. Patients underwent early (1.1 days) and follow-up (1 year) coronary angiography.	No. of centres: single centre		
11.	Choi *et al.* 2021 Korea	Cohort (n=1,043) Intervention: TTFM (Medistim; device not reported) and post-operative early coronary angiography (timepoint undefined) Comparator: N/A	Patients undergoing isolated off-pump CABG. Recruitment period between January 2010 and June 2017. Exclusion criteria: concomitant cardiac or non-cardiac procedures, aortic manipulation. No. of centres: single centre	Operative mortality, stroke, renal failure, reoperation, deep sternal infection	Main focus of paper was to evaluate risk prediction scoring systems (STS risk model, EuroSCORE II) calculated retrospectively before January 2016, and prospectively after January 2016. Mixture of techniques: SV harvested with minimal manipulation prior to October 2013, and no touch technique after. Timing of outcomes unclear.

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
12.	Davierwala *et al.* 2021a Germany	Cohort – retrospective (n=88) Intervention: TTFM (Medistim; device not reported), coronary or CT angiography (assumed prioer to discharge) performed in all patients in early part of series, and only in the presence of ischaemia in later part of the series. Comparator: N/A	Consecutive patients undergoing off-pump minimally invasive CABG. Recruitment period between February 2015 and March 2019. Exclusion criteria: patients undergoing minimally invasive direct coronary artery bypass, patients undergoing CABG due to intolerance to single-lung ventilation after induction of anaesthesia before skin incision. No. of centres: single centre	In-hospital death, 30-day mortality, low cardiac output syndrome, ECMO, MI, graft patency, bypass revision, re-exploration for bleeding, stroke, new dialysis, respiratory complications, new-onset AF, chest wound infection. Long-term outcomes: death, PCI.	List of preferable patient characteristics listed in Appendix E1 of paper.
13.	Davierwala *et al.* 2021b Germany	Cohort – retrospective (n=2,667) Intervention: MiraQ (Medistim), coronary angiography (assumed intraoperatively) Comparator: N/A	Patients undergoing elective or urgent minimally invasive direct coronary artery bypass. All patients underwent LITA graft to LAD through left anterior small thoracotomy. Patients who underwent an additional graft to the diagonal branch were also included. Recruitment period between May 1996 and December 2018. Exclusion criteria: patients who underwent minimally invasive RITA graft to the RCA through a right anterior mini-thoracotomy, minimally invasive multi-vessel CABG, totally endoscopic CABG,LITA-LAD grafting through a sternotomy because of intolerance to	Post-operative outcomes: low ouput syndrome, IABP insertion, MI, re-exploration for bleeding, new dialysis, deep chest wound infection; bypass revision, mortality (in-hospital, 5, 10, 15 and 20 years)	Subgroup analysis by date of CABG (1996 to 2003, 2004 to 2010, 2011 to 2018)

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
			single-lung ventilation after induction of anaesthesia but before skin incision. No. of centres: single centre		
14.	Dayan *et al.* 2018 Uruguay	Cohort – retrospective (n=282) Intervention: VeriQ (Medistim) Comparator: N/A	Patients with stable angina who underwent isolated CABG, through median sternotomy with cardiopulmonary bypass. Recruitment period between January 2006 and December 2014. Exclusion criteria: emergency or urgent surgery, left main stenosis. No. of centres: single centre	Post-operative outcomes (mortality, haemodialysis, pneumonia, stroke, TIA), mortality (up to 10 years)	No follow-up angiography. Focus is on benefit of pre-operative beta-blockers.
15.	De Leon *et al.* 2020 ǂUruguay	Cohort – retrospective (n=177) Intervention: VeriQ (Medistim) Comparator: N/A	Consecutive patients with three-vessel CAD who underwent isolated CABG and received at least one graft to the LAD, first OM artery, or PDA. Recruitment period between 1 January 2006 and 31 December 2006. Exclusion criteria: none used No. of centres: single centreǂ	Graft revision, operative mortality (within 30 days), new PCI and survival.	
16.	Dreifaldt *et al.* 2013 Sweden	RCT (n=108) Intervention: no touch SVG graft and RA graft to the left coronary territory Comparator: no touch SVG graft and RA graft	Consecutive patients with at least three vessel CAD, undergoing elective, first-time, CABG. Each patient received one LITA, one RA and one no-touch SVG as conduit material. Recruitment period between January 2004 and August 2009. Exclusion criteria: patients aged over 65 years, LVEF <40%, serum creatinine >120	Graft patency, peri-operative or post-operative events (MI, deaths, revascularisation)	Assumed from abstract that angiography conducted at 36 months follow-up.

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
		to the right coronary territory TTFM with VeriQ (Medistim), coronary angiography (3 years)	µmol/L, use of anticoagulants, coagulopathy, allergy to contrast medium, positive Allen's test result, abnormal result of Doppler study of the arms, history of vasculitis or Raynaud's syndrome, bilateral varicose veins or previous vein stripping. No. of centres: single centre		
17.	Erdem *et al.* 2015* Turkey	RCT (n=140) Intervention (n=70): CABG, diltiazem infusion following anaesthesia induction and intubation (2.5 microgram/kg/min), VeriQ (Medistim) Comparator (n=70): CABG, VeriQ (Medistim)	Patients with CAD undergoing surgery between March 2013 and July 2013. CABG performed according to ACC/AHA guidelines. Exclusion criteria (pre-operative): patients with poor ventricular function (ejection fraction ≤40%), resting sinusal bradycardia (<55 beats/min), left bundle branch block. Exclusion criteria (intraoperatively): haemodynamically unstable patients who required infusion of study drugs beyond the ranges of study protocol, off-pump CABG, valve and additional aortic and non-cardiac surgery. No. of centres: single centre	Graft patency (using mean graft flow and PI), need for immediate revision, prolonged intubation, AF, post-operative early MI, post-operative development of acute renal failure and need for haemodialysis, neurological complications, time spent in intensive care, in-hospital mortality.	Aim of RCT is to determine impact of diltiazem infusion of TTFM. All patients were monitored continuously for a minimum of 24 h.
18.	Gao *et al.* 2021 ǂChina	Cohort (n=52) Intervention: CardioMed Trace System (pre-dates VeriQ/MiraQ) intraoperatively.	Patients diagnosed with multi-vessel CAD (confirmed by coronary angiography pre-operatively), scheduled for CABG between April 2016 and July 2016. Exclusion criteria: congenital coronary malformations, previous history of cardiac surgery, patients without LIMA, existing	Cardiac arrhythmia, in-hospital and 30-day mortality, reintervention for ischaemic events at 3 months, measurement accuracy	Mortality only reported up to 30-days (not long term).

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
		Comparator: Colour doppler ultrasonography (TOSHIBA) was also conducted pre-operatively and at 5 to 8 days follow-up.	proximal anastomosis of LIMA on the aorta, undergone coronary endarterectomy. No. of centres: single centre	(correlation of flow characteristics between TTFM and colour doppler).	
19.	Gestrich *et al.* 2020 ŧGermany	Cohort – retrospective (n=404) Intervention: TTFM via QuickFit probe (Medistim) Comparator: N/A	Patients who underwent isolated on-pump CABG with at least one chronic total occlusion in the preoperative angiogram. LIMA used as graft to revascularise the LADartery and venous grafts, primarily the great SV , were used as single vessels to revascularise the left circumflex artery and RCA territories. Recruitment period between 2014 and 2016. Exclusion criteria: prior CABG, emergency CABG due to coronary dissection during PCI, off-pump CABG, other additional surgical procedure other than CABG. No. of centres: single centre	Blood flow (ml/min) by Rentrop grade (0 to 3)	Includes multiple linear regression analysis to determine predictors of graft flow in patients with chronic total occlusion and different Rentrop scores.
20.	Girish Gowda *et al.* 2019 India	Cohort (n=NR, 48 grafts) Intervention: VeriQC (Medistim) Comparator: Free flow measurement (collecting blood for 15 seconds).	Consecutive patients undergoing elective myocardial revascularisation using SVG as one of the conduits. Study dates not reported. Exclusion criteria: not reported No. of centres: single centreŧ	Measurement accuracy (Bland-Altman)	TTFM was measured simultaneously during free flow calculation.

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
21.	Guo *et al.* 2019 China	Cohort – retrospective (n=155) Intervention: VeriQ (Medistim), and follow-up doppler echocardiography and CT angiography (3 months post-operatively) Comparator: N/A	Patients with left main coronary artery and triple-vessel disease, or only triple-vessel disease, who underwent BIMA grafting. All surgeries conducted via median sternotomy. Recruitment period between December 2015 and August 2017. Exclusion criteria: emergency surgery or other severe cardiac diseases requiring concurrent surgery, severe heart failure or multiple organ dysfunction before the operation, pre-operative CT angiography showing proximal subclavian artery or internal mammary artery stenosis. No. of centres: single centre	Repeat CABG (3 months), graft patency, short term complications (bleeding requiring re-exploration, chylothorax, death, sternal wound complication).	Subgroup by age (less than 60 years, and 60 to 75 years)
22.	Han *et al.* 2021 China	Cohort – retrospective (n=74) Patients subgrouped into the different target territories that the RIMA was grafted to; bilateral (n=20), left (n=54). Intervention: VeriQ (Medistim) Comparator: N/A	Data extracted from database, from patients who underwent isolated CABG, through a median full sternotomy, with BIMA with different configurations, between 1 January 2018 and 31 July 2020. Exclusion criteria: CAD unsuitable or unnecessary for BIMA, combined with subclavian artery stenosis, preoperative IMA ultrasound that indicated that the IMA was fine, narrow or calcified, with concomitant additional procedures. No. of centres: single centre	Graft failure, in-hospital death, complications.	Post-operative coronary CT angiography prior to discharge. Comparison of flow parameters between bilateral and left subgroups.

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
23.	Handa *et al.* 2016 ŧJapan	Cohort – retrospective (n=68) Intervention: VeriQ (Medistim) and near-infrared ICG fluorescence imaging (Hyper-Eye Medical Systems); although HEMS evaluation not included in study outcomes Comparator: coronary angiography at 1 year (unless graft incompetence suspected by abnormal intraoperative assessment or postoperative clinical symptoms).	Consecutive patients who underwent isolated CABG with complete TTFM, HEMS and post-operative angiographic assessment. Aortocoronary bypass grafts included in analysis. Exclusion criteria: not reported No. of centres: not reported (assumed single centre as authors mention “our institution”)	TTFM classification: normal (MF>15ml/min, P<5, and DF>50%), abnormal (MF<15ml/min, PI>5, DF<50%) Coronary angiography classification: patent graft (no occlusion or graft stenosis <75% and global lesion perfusion area), failing graft (occlusion, string graft, severe graft stenosis >75% and narrow lesion perfusion area). Graft failure (subgroup analysis for TTFM and angiography classification combinations)	Occlusive grafts (no quantifiable flow) were excluded because these grafts were revised intraoperatively and pre-revision TTFM data were not saved in a part of the revision grafts. McNemar’s test used to compare intraoperative TTFM results with angiography results at 1 year (predictive).
24.	Harahsheh *et al.* 2012 Jordan	Cohort – prospective (n=436) Intervention: VQ-1101 (Medistim); the EAC	Consecutive patients undergoing CABG. Recruitment period between August 2008 and January 2009. Exclusion criteria: not reported	Graft failure (suboptimal grafts), revision	Subgroup by type of bypass. Data for revisions is in discussion not results section.

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
		assumes this is the VeriQ device. Comparator: N/A	No. of centres: single centre		
25.	Hashim *et al.* 2018 Malaysia	Cohort (n=60) Intervention: VeriQ (Medistim) Comparator: N/A	Patients undergoing IMA-coronary artery anastomosis, using novel TTFM technique to exclude error. Recruitment period from May 2016 (end date not reported). Exclusion criteria: not reported No. of centres: not reported	Graft revision, peri-operative clinical events.	
26.	Hellmann *et al.* 2020 Poland	Cohort – prospective (n=26) Intervention: VeriQ (Medistim) Comparator: LDF	Patients undergoing off-pump coronary artery surgery through a median sternotomy. Recruitment period between November 2018 and April 2019. Exclusion criteria: not reported No. of centres: not reported	Correlation (between myocardial perfusion after CABG assessed by LDF and blood flow in the coronary bypass grafts measured by TTFM)	One patient required on-pump beating heart (assumed conversion)
27.	Hiraoka *et al.* 2017 Japan	Cohort – retrospective (n=63) Intervention: VeriQ (Medistim) Comparator: multi-slice CT angiography (prior to discharge unless chronic kidney disease of grade 3 or higher)	Consecutive patients undergoing isolated CABG. Patients underwent off-pump CABG, full median sternotomy, use of arterial conduits and complete revascularisation under end-tracheal intubation, general anaesthesia and right heart catheter monitoring. Recruitment period between January 2014 and December 2014. Exclusion criteria: Patients without CT angiography within 14 days post-	Mortality (in-hospital, 30 days), peri-operative complications (AF, late cardiac tamponade, re-exploration for bleeding, surgical site infection, prolonged ventilation), reintervention for	

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
			operatively, patients with composite graft, grafts with sequential anastomosis No. of centres: single centre	ischaemic events (3 months), follow-up mortality or major cardiac adverse events including requirement for PCI for new lesions, correlation between TTFM and CT angiography.	
28.	Honda *et al.* 2015* ŧJapan	Cohort – retrospective (n=72) Intervention: VeriQ (Medistim), fluorescence graft imaging with ICG (intraoperatively). Patients also underwent post-operative imaging (within one year of surgery): multi-slice cardiac CT in patients without chronic kidney disease, plane MRI in patients with chronic kidney disease, coronary angiography used in some patients (proportion and criteria for use not defined).	Patients eligible for CABG. Patients underwent coronary angiography and FFR-based functional evaluation of mild-to-moderate stenosis of the LAD artery. Patients divided into 3 groups according to their pre-operative FFR: Group S (FFR<0.70) with the most severe coronary stenosis, Group M (0.70≤FFR<0.75) had mild stenosis, and Group N (FFR≥0.75) had functionally non-stenotic lesions. In situ ITA to LAD artery bypass performed in all patients. Revascularization of the coronary artery was performed with or without cardiopulmonary bypass. An in situ ITA (both right and left ITA) was used as a bypass graft to the LAD artery area. No Y or T grafts were used in this study. Study dates not reported. Exclusion criteria: not reported No. of centres: not reported	Intraoperative graft failure, revision, post-operative graft failure (within 1 year), mid-term mortality (953 days follow-up)	

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
		Comparator: N/A			
29.	Honda *et al.* 2019a Japan	Cohort – retrospective (n=155) Intervention: VeriQ (Medistim), IFI Comparator: pre- and post-operative transthoracic echocardiography (CFVR) via high-frequency colour Doppler and pulse wave Doppler (mean 9.6 months) Multi-slice CT angiography (n=147), MRI (n=6), or coronary angiography (n=2) used during follow-up (mean 13.1 months)	Patients undergoing isolated CABG. Recruitment period between June 2008 and July 2017. Exclusion criteria: emergent and urgent cases, history of asthma, drug allergy for adenosine triphosphate, total or subtotal occlusion of the LAD, LAD revascularisation other than the "in situ" ITA graft, without preoperative coronary flow velocity reserve (CFVR), without postoperative CFVR, undergoing concomitant surgery No. of centres: single centre	Correlation (preoperative left ventricular mass gained from preoperative echo examinations and intraoperative graft flow), death (follow-up).	Subgroup analysis: patients with and without left ventricular hypertrophy Overlap with Honda *et al.* 2019b.
30.	Honda *et al.* 2019b Japan	Cohort – retrospective (n=161) Intervention: VeriQ (Medistim), IFI	Patients undergoing isolated CABG. Recruitment period: June 2008 and December 2017. Exclusion criteria: emergent and urgent cases, history of asthma, drug allergy for adenosine triphosphate, total or subtotal	Death (follow-up).	Subgroup analysis: patients with and without haemodialysis.

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
		Comparator: pre-and post-operative transthoracic echocardiographic examination (CFVR) via high-frequency colour Doppler and pulse wave Doppler (median 83 days) Multi-slice CT angiography, or MRI used during follow-up for graft evaluation (median 91 days).	occlusion of the LAD artery, patients undergoing LAD revascularisation other than the "in situ" ITA graft, sequential grafts, without preoperative CFVR, without postoperative CFVR, undergoing concomitant surgery. No. of centres: single centre		Overlap with Honda *et al.* 2019a.
31.	Hosono *et al.* 2020 ŧJapan	Cohort – retrospective (n=24) Intervention: TTFM (Medistim), coronary or multi-slice CT angiography (post-operative) in some patients Comparator: N/A	Patient undergoing solitary CABG using a free RITA proximally anastomosed to an SVG. Recruitment from June 2016 (end date not reported). Exclusion criteria: combined surgery, redo surgery No. of centres: single centreŧ	In-hospital outcomes (death, mediastinitis, prolonged mechanical ventilation, re-exploration for bleeding, renal dysfunction, low output syndrome, cerebrovascular complications), graft patency (post-operatively, timepoint not defined).	Subgroup analysis: flow measured before and after clamping in RITA and SVG separately, individual versus sequential.

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
32.	Hwang *et al.* 2018 ŧKorea	Cohort – prospective (n=23) Intervention: TTFM (Medistim), diameter and endothelial shear rate measured using ultrasound, coronary or multi-slice CT angiography (1 year), intra-graft Doppler-guidewire performed after angiography (1 year, only in 6 patients). Comparator: N/A	Patients scheduled to undergo primary isolated off-pump CABG using a SV Y-composite graft based on the in situ left ITA in an operating theatre equipped with the probe used to evaluate cross-sectional images of the bypass conduits. Recruitment between October 2012 and December 2013. Exclusion criteria: urgent or emergent procedures, malignant disease that would limit 1-year follow-up, chronic renal failure which might limit angiographic follow-up. No. of centres: single centreŧ	Graft patency (early-timepoint undefined, 1 year), complications (MI, conduit injury) at 1 year follow-up.	Subgroup analysis: MF through proximal ITA, distal ITA, and SV conduits. Uni- and multi-variate analysis to determine whether intraoperative flow was associated with conduit diameter.
33.	Inderbitzin *et al.* 2015* ŧSwitzerland	Cohort - prospective (n=22) Intervention: MiraQ (confirmed by corresponding author), CT angiography conducted at one year post-surgery. Comparator: N/A	Consecutive patients receiving eSVS (external venous nitinol mesh) meshed SVG. Recruitment between June 2010 and June 2011. All patients underwent off-pump CABG with conventional ECC/minimal ECMO. Each patient received one eSVS meshed SVG either to the left or right coronary system grafted to either single coronary vessel (one single DAS) or to two or more coronaries (sequential distal anastomoses). A stenosis of >75% was considered indispensable for being grafted. The LAD was routinely grafted using the LIMA. Coronary run-off was classified as poor (calcified vessel AND diameter ≤1.5 mm),	Primary: graft patency on CT angiography Secondary: device-related complications, post-operative complications (including MACCE).	Three patients died prior to one-year follow-up and were excluded from analysis. Corresponding author contacted 17/02/2022; reply received 17/02/2022.

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
			moderate (calcified vessel OR diameter ≤1.5 mm) or good (not calcified vessel AND diameter >1.5 mm). The residual coronaries with significant stenosis (>75%) were grafted using the LIMA or RIMA, the RA or an unmeshed SVG. Exclusion criteria: Graft diameters >7 mm and <3.6 mm as well as a double wall thickness >1.4 mm were contraindications to eSVS mesh. No. of centres: not reported		
34.	Jiang *et al.* 2020 China [NCT03126409]	RCT; block randomisation (n=59) Intervention (n=30): "no-touch" SVG harvest technique Comparator (n=29): conventional SVG harvest technique All patients underwent TTFM measurement by VeriQ (Medistim) and multi-slice CT angiography before discharge	Consecutive patients with CAD. All included patients had triple vessel disease, underwent LIMA anastomosed to LAD artery and a sequential SVG onto the other three coronary arteries at the left side of the heart with target run-off ≤2mm. Recruitment period between October 2017 and December 2017. Exclusion criteria: emergency coronary bypass surgery, concomitant valve or aortic surgery, sever poor-quality SVGs, ventricular aneurysm, without multi-slice CT angiogram evaluation before discharge, average run off >2mm. No. of centres: single centre	Graft patency, cerebrovascular events in hospital	Focus on technique (TTFM measured in all patients). Patency verified by multi-slice CT angiography.

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
35.	Joshi *et al.* 2020 ǂIndia	Cohort – prospective (n=40) Intervention: TEE Comparator: VeriQ (Medistim; standard of care).	Consecutive adult patients scheduled for elective CABG under cardiopulmonary bypass support. Study dates not reported. Exclusion criteria: LVEF<50%, associated valvular lesions, complications after MI such as ventricular septal rupture or LV aneurysm, emergency CABG, dilated coronary sinus (>1cm diameter) No. of centres: single centre	Graft revision (based on TTFM: mean PI>5, mean DF<50%).	TTFM used as comparator as standard of care, TTFM defined outcome (need for revision) and subgroups, and intervention was TEE.
36.	Kaya *et al.* 2018 ǂTurkey	Cohort – retrospective (n=1,240) Intervention: VQ-1101 (Medistim), electrocardiography Comparator: N/A	Patients who underwent median sternotomy and pump-isolated CABG. Recruitment period between January 2007 and March 2017. [Note TTFM introduced from 2006 from abstract]. Exclusion criteria: coronary bypass together with other cardiac surgical operations, off-pump CABG No. of centres: single centre	Graft revision (peri-operative) and causes of revision, post-operative outcomes (re-exploration for bleeding, deep sternal infection, IABP placement, peri- or post-operative infarction), mortality	ROC analysis to estimate early graft failure.
37.	Kim *et al.* 2020a ǂKorea	Cohort - retrospective (n=2,919) Intervention: TTFM (device not named; Medistim) from October 2000 (n=2,599). Follow-up angiography (≤7 days, n=2,820).	Consecutive patients undergoing off-pump CABG. Recruitment between 1998 and 2017. Exclusion criteria: patients who had died, refused angiographic evaluation, post-operative development of acute renal failure excluded from angiographic follow-up.	Mortality (within hospitalisation or within 30 days of procedure), AF, respiratory complications, post-operative acute renal failure, stroke, perioperative MI, patency, revisions.	Patients recruited over 20 years, but short follow-up. Revascularisation strategies changed during study period.

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
		Subgroup: by time (1998-2007 [n=1,345] and 2008-2017 [n=1,574]) and inclusion of TTFM (pre-TTFM, post-TTFM)	No. of centres: single-centre (assumed from single affiliation for all authors)		Potential overlap with Kim *et al.* 2021; unconfirmed
38.	Kim *et al.* 2021 Korea	Cohort – retrospective (n=1,283) Intervention: intraoperative TTFM (Medistim; device not reported), coronary angiography (mean 1.4 days, 1 year)	Patients undergoing isolated off-pump CABG, receiving no-touch SV conduit as a Y- or I-composite graft based on the in situ left ITA for myocardial revascularisation, with early post-operative angiogram. Recruitment between January 2008 and December 2018. Exclusion criteria: early post-operative angiogram not available, on-pump CABG, SVG not used, SVG composite graft based on right ITA or RGEA, free SVG No. of centres: single centre	Graft patency	Study focuses on follow-up of occluded grafts.
39.	Kornovski *et al.* 2017 Bulgaria	Cohort (n=64) Intervention: VeriQ (Medistim) Comparator: N/A	Inclusion and exclusion criteria not reported. Recruitment between 2014 and 2016. No. of centres: single centre	Graft failure, revision, cardiogenic shock	Subgroup analysis by off-pump and on-pump
40.	Kuroyanagi *et al.* 2012 Japan	Cohort – retrospective (n=159) Intervention: VeriQC or Butterfly flowmeter (Medistim) and	Consecutive patients undergoing off-pump CABG. Recruitment period between April 2009 and November 2011. Exclusion criteria: not reported	Graft failure, revision	Subgroup by type of graft (RITA, LITA, GEA, SVG). Some patients had coronary angiography

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
		indocynanine green and SPY system (both intraoperatively), coronary angiography (n=31) or CT angiography (n=128) (approx. 1 week) Comparator: N/A	No. of centres: single centre		(n=31), the rest had CT angiography which may influence results.
41.	Laali *et al.* 2021 ~~I~~France	Cohort – retrospective (n=925) Intervention: TTFM (Medistim; device not reported) Comparator: No TTFM	Patients undergoing total arterial CABG with ITAs. Complete arterial revascularisation with a single or bilateral ITA with a Y-configuration was planned for all patients. Recruitment period between January 2017 and February 2020. Exclusion criteria: critical pre-operative status according to Euroscore II definition, redo procedures. No. of centres: not reported	Time for procedure, graft revision, mortality, adverse events	Subgroup analysis patients with TTFM assessed and those not (surgeon preference) Multivariate analysis.
42.	Lee *et al.* 2020 Korea [Korean Clinical Trials Registry: KCT0002047]	Cohort – prospective (n=57) Intervention: VeriQ (Medistim) Comparator: N/A	Patients undergoing on-pump or off-pump CABG. Recruitment period between July 2016 and May 2018. All patients underwent median sternotomy. All patients were transferred to ICU after surgery and moved back to general ward when stable. Exclusion criteria: emergency surgery, poor left ventricular systolic function (preoperative ejection fraction <40% on echocardiogram), had not undergone LIMA to LAD anastomosis, had	Post-operative complications, MI, AF, wound complication, AKI, death	Study includes regression analysis to investigate peri-operative factors which may impact TTFM.

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
			preoperative arrhythmias such as AF, refused participation, had no blood viscosity measurements taken, or had PI>5. Minimal invasive surgery was excluded for consistency of surgical procedures. No. of centres: single centre		
43.	Li *et al.* 2021a China	Cohort – prospective (n=259) Intervention: VeriQ (Medistim) twice for each graft, multi-slice CT angiography (1 year), electrocardiography and echocardiography (during follow-up, timepoint undefined) Comparator: N/A	Patient undergoing off-pump CABG with the use of at least one sequential venous graft to the RCA system. All patients were triple-vessel coronary heart disease, and the stenosis of RCA system (≥75%) limitation lies in the proximal or middle segment of the RCA without affecting the opening of PDA and posterior left ventricular branch. Recruitment period between August 2014 and August 2019. Exclusion criteria: not reported No. of centres: single centre	Complications (within 30 days), graft patency	Subgroup analysis by a) different locations of anastomoses (LIMA, SV) b) different coronary systems (LAD, circumflex artery, RCA) Potential overlap Li *et al.* 2021b; unconfirmed
44.	Li *et al.* 2021b China	Cohort – retrospective (n=200) Intervention: TTFM (Medistim), CT angiography (6 months, 12 months, annually thereafter), coronary angiography if	Patients with a PDA severe lesion who underwent off-pump CABG and coronary endartectomy (n=95) and those coupled with DAS for anastomosis of SVG-PDA (n=105). Recruitment between January 2016 and December 2018. Exclusion criteria: CE to other sites	Mortality (peri-operatively, 30 days, mid-term), graft patency, clinical events (angina, death, MACCE, non-fatal MI, cerebrovascular accident, hospitalisation for	Subgroup analysis by off-pump CABG with coronary endarterectomy with and without DAS

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
		required to determine need for PCI Comparator: N/A	No. of centres: not reported (single surgeon)	heart failure, need for revascularisation) up to 36 months.	KM for graft patency (by subgroup). Potential overlap with Li *et al.* 2021a; unconfirmed
45.	Lobo *et al.* 2016 Brazil	Cohort – prospective (n=23) Intervention: Butterfly flowmeter (Medistim) Comparator: N/A	Patients undergoing off-pump elective CABG through median sternotomy (without associated procedures) with arteriovenous composite Y-grafts revascularising anterior interventricular artery and another branch of left coronary system. Recruitment period between July 2013 and June 2015. Exclusion criteria: patients diagnosed with diffuse CAD, patients who underwent associated procedures. No. of centres: single centre	Complications, acute MI, need for IABP , cerebrovascular accident, acute renal failure, mediastinitis, osteomyelitis, sepsis, clinical evidence of ischemia.	
46.	Mahmoud *et al.* 2017 ŧEgypt	Cohort - retrospective (n=400) Intervention: TTFM (Medistim; device not reported), echocardiography (pre- and 1 week, 3, 6, 12, 24 months), TEE (intraoperatively)	Patients with ischemic heart disease with EF≤35% undergoing CABG, on-pump (n=200) and off-pump (n=200). In all patients in both groups, used pedicled LIMA to an average sized LAD and vein grafts to the rest of the left and right systems. The RA and bilateral LIMA were not used. In all cases used standard median full sternotomy, cannulating the ascending aorta excluding any area with heavy aortic atherosclerosis. Recruitment	Clinical events (peri-operatively: mortality, post-operatively: heart failure, stroke, re-exploration, transfusion, renal impairment, hepatic impairment, wound infection, mortality)	Follow-up imaging only mentioned in abstract (not methods section). Duration of follow-up not reported (unclear timepoint of clinical events reported in table 3).

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
		Comparator: N/A	period between January 2012 and December 2014. Exclusion criteria: recent MI, associated significant carotid artery disease, associated ventricular aneurysm, heart failure, recent or old strokes, femoral arterial block, incompletely re-vascularised patients, bad LAD or no LIMA to LAD, associated renal failure or impairment, associated valve lesions, redo cases. No. of centres: multi-centre (N=NR)		
47.	Martinovic *et al.* 2019 ŧCroatia, Germany	Cohort (n=12) Intervention: VeriQC (Medistim), electrocardiography (4 times during admission), echocardiography (preoperatively, intraoperatively, at discharge), coronary angiography only conducted in patients who fulfilled corresponding criteria (undefined)	Patients with major coronary artery stenosis (75% angiographic diameter stenosis) limited to a double coronary distribution on the anterior and inferior surface of the heart were selected for revascularisation using minimally invasive direct approach through the distal mini-sternotomy approach. All patients had LAD or diagonal branch and RCA disease or both. All patients received arterial grafts. Recruitment period between January 2016 and January 2017. Exclusion criteria: presence of major CAD on lateral surface of the heart, acute MI requiring intravenous administration of nitrates or an IABP. No. of centres: not reported (single surgeon)	Clinical events, mean total operative time (single arm)	Main focus on new surgical approach. No reporting of MF as outcome measure, but used TTFM during procedure.

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
48.	Mohamed *et al.* 2019 Kuwait	Cohort – prospective (n=50) Intervention: VeriQC (Medistim), multi-slice CT angiography (n=8 randomly selected patients who had their respective RA analysed histologically at the time of harvest), coronary angiography (n=4 with recurrence of angina or MI postoperatively). Comparator: N/A	Consecutive patients aged over 18 years, undergoing first time isolated CABG utilising RA as a conduit. Additional inclusion criteria: life expectancy more than 2 years, absent contrast allergy, non-emergency CABG, absence of contraindications to RA harvest, presence of non-dominant left arm, normal kidney function, and suitable coronary anatomy. Eligibility for RA harvest included non-dominant hand used for harvest, Allen test <6 seconds the day before surgery in the arm harvest site, pulse oximetry examination just prior to radial harvest must normal after occlusion of RA , suitable target vessel (>1 mm). Recruitment period between 1 February 2015 and 1 March 2016. Exclusion criteria: not reported No. of centres: multi-centre (N=2)	Complications relating to harvest site, mortality (30 days, 1 year), repeat vascularisation (PCI, 1 year), graft patency (1 year, n=8 only)	Flow measurements not available in 6 patients (see Table 1). Follow-up angiography selective (not in all patients).
49.	Monsefi *et al.* 2016 ŧGermany	Cohort (n=147) Intervention: VeriQ (Medistim), multi-slice CT and coronary angiography Comparator: N/A	Patients with CAD undergoing elective CABG using valvulotomised venous graft to the RCA. Recruitment period between November 2007 and January 2010. Exclusion criteria: not reported No. of centres: single centre (ŧ, single surgeon)	Mortality (in-hospital, 30 days, follow-up), MI, graft patency, reintervention	Patency measured in subset using different techniques: 45 multi-slice CT and only 5 reangiography. Comparison of flow before and

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
					after grafting in subset (n=12)
50.	Nakajima *et al.* 2016 ~~ł~~Japan	Cohort - retrospective (n=32) Intervention: TTFM (Medistim; device not reported) and CT angiography or coronary angiography (approx. 2 weeks) in patients without renal dysfunction or other comorbidity. Comparator: N/A	Patients underwent off-pump CABG with IABP. Recruitment period between January 2011 and May 2015. Exclusion criteria: not reported No. of centres: not reported (assumed single centre as authors mention “our institution”)	Graft patency	Coronary angiography only conducted in patients without renal dysfunction or other comorbidity such as severe calcification of the aorta or sever chronic obstructive pulmonary disease.
51.	Nakajima *et al.* 2018 ~~ł~~Japan	Cohort – retrospective (n=405) Intervention: TTFM (Medistim; device not reported) and postoperative coronary angiography. Comparator: N/A	Patients with bypass grafts who had undergone off-pump CABG and had postoperative coronary angiogram. Recruitment period between 2007 and May 2015. Bypass grafts that were individual and created as the sole bypass graft for the relevant vascular region were included. Patients were consecutive after exclusion of those without eligible bypass grafts. Exclusion criteria: not reported beyond those grafts not individual or the sole bypass graft for the relevant vascular region.	Graft failure	Coronary angiography performed postoperatively (time point not explicitly defined, assumed on completion).

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
			No. of centres: single centre (assumed from single affiliation for all authors)		
52.	Nakajima *et al.* 2019 ~~ł~~Japan	Cohort – retrospective (n=230) Intervention: TTFM (Medistim; device not reported), coronary angiography (mean 1.5 months, less than 1 month in 93% of patients) Comparator: N/A	Patients undergoing off-pump CABG, with SVG or GA used for RCA revascularisation, created as the sole bypass graft. Recruitment between July 2007 and December 2015. Exclusion criteria: other graft materials, composite or sequential grafts No. of centres: single centre~~ł~~	Graft failure, competitive flow, technical error in flow measurement	Graft failure defined as occlusion or string sign (diffuse narrowing of the graft) by catheter selective angiography. Subgroup by SVG or GEA graft
53.	Nakamura *et al.* 2019 Japan	Cohort – prospective (n=393) Intervention: VeriQ (Medistim), coronary angiography and echocardiography, CT and MRI (to confirm neurologic events), single photon emission CT (in cases of carotid artery stenosis). Comparator: N/A	Patients undergoing isolated CABG. Prior to all CABG, MDT to discuss the indication for preoperative and prophylactic IABP in high-risk patients. High risk defined as NYHA class III or IV, LVEF <40%, left-ventricular end-diastolic internal diameter >65mm, left main stenosis >50%, diffuse CAD (requiring three or more distal anastomoses), refractory unstable angina. Recruitment between December 2005 and December 2017. Exclusion criteria: contraindication to IABP (defined as severe peripheral vascular disease, aortic regurgitation, dissection or aneurysm)	In-hospital complications, mortality (in-hospital, 30 days, 12 months), MACCE (30 days, 1 year)	Subgroup by presence of prophylactic IABP. Use of echocardiography and coronary angiography (beyond its use for placement of IABP) reported in discussion, not methods.

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
			No. of centres: single-centre		
54.	Navia *et al.* 2016 Argentina	Cohort – retrospective (n=3,757) Intervention: VeriQ (Medistim), postoperative (assumed coronary) angiography (timepoint NR) Comparator: N/A	Consecutive patients undergoing exclusively CABG, either urgent or elective. Patients were included if they had 2 or 3 vessel CAD and received at least 1 ITA graft in situ. Recruitment period between November 1996 and May 2014. Exclusion criteria: not reported No. of centres: single centre	Early outcomes (30-day mortality, deep sternal wound infection, post-operative MI, post-operative stroke, reoperation for bleeding, acute renal impairment requiring dialysis), long-term survival and events (new acute MI or need for PCI, or both)	Subgroup analysis of BITA grafting in a T-configuration exclusively (n=2,098) versus using SITA grafting (n=1,659) in patients with multi-vessel disease. Study includes propensity matched cohorts (n=485 in each arm). SITA further subgrouped into patients who underwent operation with LITA and RA with or without additional SVG (n=1,242), and patients receiving LITA

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
					supplemented by SVG only (n=388)
55.	Niclauss *et al.* 2020 ŧSwitzerland	Cohort – prospective (n=35) Intervention: VeriQC and QuickFit TTFM probe (Medistim), coronary angiography (timing not explicitly reported), cardiac MRI (6 to 12 weeks) Comparator: N/A	Consecutive patients undergoing off-pump CABG by same surgeon. LIMA used in all patients, followed by RIMA, principally used as a second graft for additional left coronary revascularisation (patients aged 75 years or less). The SV was used as third graft to the RCA, the PDA or in older patients (aged greater than 75 years) also as a second graft to left coronary branches. Median sternotomy approach used. Left anterior mini-thoracotomy preferred for isolated LIMA to LAD bypasses. Exclusion criteria: emergency or salvage procedures, pre-existing rhythm disorders (chronic AF that impedes cardiac MRI analysis), MRI contra-indications (pacemaker leads, claustrophobia). No. of centres: not reported	In-hospital adverse events (death, acute perioperative MI), out of hospital death, rehospitalisation, myocardial ischaemia	Assumed that all patients underwent coronary angiography and cardiac MRI; however not explicitly reported.
56.	Oshima *et al.* 2016 ŧJapan	Cohort – retrospective (n=196) Intervention: VeriQ (Medistim) Comparator: coronary angiography (1 month),	Patients undergoing isolated CABG, either with or without cardiopulmonary bypass. Only patients with intraoperative TTFM and post-operative coronary angiogram. Recruitment period between January 2009 and October 2015. Exclusion criteria: not reported	Graft failure, including regression analysis to determine predictors.	Study compares TTFM and Rentrop collateral grade between patent and failed grafts (outcome from coronary angiogram), and

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
		Rentrop grade (pre-operatively)	No. of centres: not reported (assumed single centre as authors mention “our institution”)		also reports correlation between pre-operative Rentrop collateral grade and intraoperative TTFM.
57.	Ozdemir *et al.* 2019 Netherlands [Trial registration: NL44701.060.13]	Prospective non-blinded RCT (n=131) Intervention (n=65): topical treatment of harvested RA with verapamil Comparator (n=66): topical treatment of harvested RA with nicardipine All patients had flow measurement taken in vivo using VeriQ4122 (Medistim)	Patients undergoing CABG with the use of the RA. Recruitment period between January 2013 and June 2017. Exclusion criteria: patients undergoing emergency operation. No. of centres: single centre	Complications (early), postoperative complications (mortality 120 days, re-exploration, MI, wound complications, circulatory complications, renal insufficiency, neurological complications, infection).	Reports mean direct flow after NaCl incubation and after incubation in the Ca+ channel blocker. MF compared between arms.
58.	Pettersen *et al.* 2017 ǂ Norway	RCT; web-based randomisation (n=100) Intervention (n=49): Pedicled vein harvesting	Patients undergoing first time non-emergent on-pump CABG after median sternotomy using SV as a conduit for revascularisation, randomly assigned to either conventional or pedicled vein harvesting. All patients were offered clinical follow-up at 6 weeks. Study dates not reported.	Post-operative complications (reoperation for bleeding, erythrocyte transfusion, plasma transfusion, thrombocyte transfusion, leg	Angiography not conducted in all patients.

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
		Comparator (n=51): conventional vein harvesting All patients had graft flow measurement with VeriQ (Medistim), first 60 patients offered 6 month angiographic follow-up including optical coherence tomography.	Exclusion criteria: insulin dependent diabetes mellitus, malignancies, acute or chronic inflammatory diseases, smoking during past 6 months, serum creatinine >120 µmol/L. No. of centres: single centre	wound infection, 30-day mortality), graft patency at 6-months.	
59.	Rasekh & Mahmoud 2021 Egypt	Cohort (n=100) Intervention: VeriQ (Medistim), echocardiography (post-operatively, timepoint NR), coronary angiography (mentioned in abstract) Comparator: N/A	Patients with multi-vessel CAD undergoing BIMA grafting. Recruitment period between January 2017 and January 2019. Exclusion criteria: emergency surgery or patients with other critical disease requiring concurrent surgery, patients with severe cardiac failure or multiple organ dysfunction before surgery. No. of centres: single centre	Operative mortality, re-exploration for drainage, dialysis, AF, prolonged ventilation, deep sternal wound infection.	Coronary angiography mentioned in abstract but not reported elsewhere.
60.	Reineke *et al.* 2012 ŧSwitzerland	Cohort – prospective (n=27) Intervention: CardioMed (Medistim) Comparator: MRI phase-contrast flow	Patients undergoing primary elective on-pump CABG. Study dates not reported. Exclusion criteria: not reported No. of centres: single centreŧ	Comparison of flow measurements between intraoperative CardioMed and MRI phase-contrast (within 1 week)	Additional detail of timing of MRI in abstract (not all in methods section). Subgroup analysis by type of bypass (RCA, RCX, diagonal artery,

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
		measurements (within 1 week)		including correlation.	marginal artery, LIMA-LAD).
61.	Rufa *et al.* 2020 ŧGermany	Cohort – retrospective (n=304) Intervention: VeriQ (Medistim) Comparator: N/A	Patients undergoing isolated CABG at least 30 days after cardiac surgery. Recruitment period between January 2006 and June 2015. Exclusion criteria: not reported No. of centres: single centre	Post-operative outcomes (new onset renal failure, stroke, deep sternal wound infection, use of IABP, use of ECMO, cardiopulmonary resuscitation, PCI, reoperation for bleeding, reoperation with bypass revision, ventricular arrhythmia), mortality (30 days, up to 10 years), neurologic events, peri-operative MI, bleeding.	Subgrouped by off-pump and on-pump. Includes propensity matched analysis. Of the 304 included patients, 269 (88.5%) had undergone previous CABG (not exclusively redo CABG).
62.	Sakabe *et al.* 2020 ŧJapan	Cohort – prospective (n=14) Intervention: VeriQ (Medistim) Comparator: Dynamic cardiac CT with CT angiography obtained	Patients undergoing primary elective CABG with TTFM and postoperative dynamic cardiac CT within 2 weeks of surgery. All SVG were harvested using an open technique, all ITA grafts harvested in a skeletonised fashion. All procedures performed through median sternotomy, standard cannulation and ECMO for on-pump procedures or with used of	Correlation (CT flow and TTFM)	

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
		as a boost scan (within 2 weeks after surgery) and visually evaluated	stabilisers for off-pump procedures. Recruitment period between July 2017 and February 2018. Exclusion criteria: poor image quality, sequential and composite grafts No. of centres: not reported		
63.	Satdhabudha *et al.* 2017 Thailand [TCTR20160913002]	RCT (n=60) Intervention (n=30): LITA harvest semiskeletonised (flow measured by VeriQ; Medistim) Comparator (n=30): LITA harvest pedicled (flow measured by VeriQ; Medistim)	Consecutive patients undergoing CABG for LAD revascularisation. Median sternotomy performed. Recruitment between July 2015 and May 2016. Exclusion criteria: emergency surgery, ejection fraction <0.5, combined cardiac associated operative procedure, left ITA diameter <1.5 mm. No. of centres: single centre (assumed from single affiliation for all authors)	Diastolic filling (TTFM), post-operative adverse events.	Graft flow measured at 5 separate circumstances (F1,F2,F5 all with TTFM; F3,F4 with free-flow). No comparison of measurements between TTFM and free-flow made.
64.	Seetharama Bhat *et al.* 2019 India	Cohort (n=424) Intervention: VeriQ (Medistim) Comparator: N/A	Patients who underwent off-pump CABG. All patients had median sternotomy, and LIMA, left or right SV harvested. LIMA was anastomosed to LAD, and SVG used for another coronary grafting. Recruitment period between July 2014 and July 2018. Exclusion criteria: not reported No. of centres: single centre	Graft patency, revision, intraoperative ST elevation, mortality	Measured flow before and after revision.

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
65.	Sharipov *et al.* 2017 Uzbekistan	Cohort – prospective (n=270) Intervention: MiraQ (Medistim) Comparator: N/A	Consecutive patients undergoing off-pump isolated CABG. Recruitment period between April 2015 and April 2017. Exclusion criteria: not reported No. of centres: single centre	Post-operative (in-hospital) outcomes: inotropic support, prolonged intubation, transfusion, AF, chest re-open for haemostasis, superficial wound infection, perioperative MI, neurological complications, mortality.	Subgroup analysis by presence of left main CAD. Surgical techniques described but graft use not well reported.
66.	Shehada *et al.* 2019 ŧGermany	Cohort – retrospective (n=112) Intervention: TTFM (Medistim; device not reported), coronary or multi-slice CT angiography Comparator: N/A	Patients with diffuse or severe CAD undergoing coronary endarterectomy within their CABG surgery, from the same surgeon. Only patients accepting postoperative coronary imaging were included. Recruitment period between May 1999 and December 2017. Exclusion criteria: not reported No. of centres: single centre (ŧ, single surgeon)	Early outcomes (up to 30 days): mortality, MI, stroke, low cardiac output syndrome, post-operative haemodialysis, respiratory insufficiency, re-exploration for bleeding, antiplatelet therapy. Long-term outcomes (imaging at mean of 53 months): graft patency, NYHA class, stroke,	All patients underwent coronary endarterectomy with CABG

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
				recurrent angina symptoms, MI, PCI, re-CABG, other cardiac surgery.	
67.	Stastny *et al.* 2021 ŧAustria	Cohort (n=134) Intervention: VeriQ (Medistim) for TTFM and EUS Comparator: N/A	Patients with multi-vessel disease undergoing on-pump coronary artery surgery, documented TTFM with an arrested heart and after weaning from bypass, at least one IMA used, documented EUS (preference of surgeon). All patients had median sternotomy, and conventional harvesting of skeletonised IMA. Recruitment period between May 2014 and September 2018. Exclusion criteria: no IMA used, required documentation not available. No. of centres: single centre (assumed from single affiliation for all authors)	Comparison of TTFM between LIMA to LAD, and RIMA to the OM, intermediate, and CX, correlation between final flow or flow with arrested heart and degree of stenosis, final PI (without bypass), size of the blood distribution area, diameter of target vessel, percentage of flow change, death, graft dysfunction and revision, stroke	Epicardial ultrasound results reported separately and not included in review.
68.	Su *et al.* 2018 China	Cohort – retrospective (n=288 after propensity matching) Intervention (n=144): lower distal mini-sternotomy off-pump CABG (TTFM measured by Medistim device)	Patients who received lower distal mini-sternotomy off-pump CABG, or standard off-pump CABG. Patients with triple-vessel coronary disease confirmed by coronary angiography, not treated by PCI, contraindicated to PCI. Recruitment period between January 2013 and January 2014. Exclusion criteria: left ventricular end-diastolic diameter index <3.2 cm/m^2,	Graft patency, peri-operative events (MI, death, blood transfusion, ICU stay, hours on ventilator) short-term outcomes (30 days: death, stroke, MI, respiratory failure or infection,	Comparison of TTFM between groups and by type of graft. Followed up to 5 years.

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
		Comparator (n=144): standard off-pump CABG (TTFM measured by Medistim device) Follow-up included echocardiogram (1 month), CT angiography (if angina-like symptoms)	grafted at the high origination of the OM coronary artery, LVEF<40%. No. of centres: single centre	renal failure, mediastinitis, AF, wound infection, re-hospitalisation), clinical events at follow-up (6 months, annually: MACCE)	
69.	Tamim *et al.* 2020 Saudi Arabia	RCT (n=50) Intervention (n=25): endoscopic harvesting of RA Comparator (n=25): open harvesting of RA All patients underwent TTFM (Medistim; device not reported) and MF and PI measurement intraoperatively, and multi-slice CT angiography (1 year) and transthoracic echocardiography (1 year), ECG (1 year)	Patients scheduled for elective isolated first time, multi-vessel CABG with use of a RA conduit as one of the grafts. Other types of conduits (LIMRA, RIMA, SVG) were utilised as required. Recruitment period between 2016 and 2018. Exclusion criteria: declined consent, uncertainty regarding attendance at one-year follow-up, borderline Allen's test, recent trans-radial catheterisation of the non-dominant hand, moderate or severe renal impairment, non-elective, urgent or emergency surgery, re-do surgery, concomitant surgery, poor LVEF (<30%), chronic renal failure already on dialysis or likely to require dialysis in future, incomplete palmar arch or inadequate collateral blood flow as assessed before surgery and intraoperatively.	Early outcomes (mortality, wound healing, major and minor neuralgias, vascular complications). Long-term outcomes, one year (hand function, patient satisfaction, mortality, MACCE, graft patency, stent insertion, major and minor neuralgias)	Statistical comparison of mean graft flow and pulsatility index between arms.

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
			No. of centres: single centre		
70.	Tamura *et al.* 2021 Japan	Cohort – retrospective (n=169) Intervention: VeriQ (Medistim), and coronary angiography (post-operatively within 14 days, in all patients without chronic kidney disease or deterioration of post-operative renal function: 127/169 patients). Comparator: N/A	Patients undergoing CABG, or CABG with aortic valve replacement. Recruitment period between February 2013 and May 2018. Endoscopic SV harvesting introduced from June 2018. Exclusion criteria: patients who received only an internal mammary artery graft, those who underwent emergency operations, and those with infective complications. No. of centres: single centre	Early outcomes (timepoint not defined): graft patency, re-sternotomy, mediastinitis, AF, re-intubation, infection of lower extremities, lymphorrhea of lower extremities, in-hospital death.	Subgroup analysis by endoscopic or open SV harvest technique.
71.	Tang *et al.* 2021 China	RCT (n=147) Intervention (n=70): aspirin and ticagrelor, TTFM measured by Medistim device Comparator (n=77): aspirin and clopidogrel, TTFM measured by Medistim device FitzGibbon grade determined by multi-	Consecutive patients undergoing elective CABG (off-pump or on-pump). Recruitment between October 2017 and December 2018. Exclusion criteria: patients with an abnormal quantity of platelets before operation (low or high), urgent CABG, previous CABG or other cardiac surgery, concomitant valve or other cardiac surgery, single vessel disease, LVEF <30% on preoperative ultrasound, infusion of fresh platelets during or after CABG, the need for perioperative warfarin, an active	Graft failure (12 months), MACCE	

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
		slice CT angiography (12-months).	gastroduodenal ulcer or postoperative gastro-intestinal bleeding, postoperative low cardiac output syndrome, perioperative MI. No. of centres: single centre		
72.	Tolegenuly *et al.* 2020 ǂLithuania	Cohort – prospective (n=25) Intervention: VeriQC (Medistim) after angiography and after revisions, coronary angiography Comparator: iFR (functional assessment of stenosis performed in cath lab and calculated as the mean pressure distal to the stenosis during the diastolic wave-free period by the mean aortic pressure during the diastolic wave-free period) for all angiographically intermediate (40% to 75% diameter) stenoses.	Consecutive patients with multi-vessel stable CAD undergoing CABG with intraoperative TTFM measurement. Performed via median sternotomy with cardiopulmonary bypass. Study dates not reported. Exclusion criteria: not reported No. of centres: not reported	Perioperative mortality, post-operative complications, graft defects, reinterventions, correlation between TTFM and iFR	Grafts subgrouped by iFR group: - Group 1 iFR<0.86 (severe coronary stenosis) - Group2 iFR 0.86-0.90 - Group 3 iFR >0.90 (non-significant)

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
73.	Tolegenuly *et al.* 2021 Lithuania	Cohort – prospective pilot (n=100) Intervention (n=50): coronary angiography with instantaneous wave-free ratio and pullback (using pressure guide wire), VeriQ (Medistim confirmed by author), CT angiography (follow-up, mean 224 days) Comparator (n=50): control group of patients who did not undergo an intraoperative graft assessment (assume this means via instantaneous wave-free ratio and pull back as TTFM was applied to all grafts)	Consecutive patients with chronic multi-vessel CAD undergoing intraoperative graft assessment by angiography in a hybrid operating room, via median sternotomy. Study dates not reported. Exclusion criteria: LVEF <30%, history of MI within last 30 days, any emergency CABG within 48 hours of the procedure, significant chronic or acute kidney, hepatic, lung disease. Contraindication for participation in our study included patients pre-operative blood creatinine level >120 µmol/L. No. of centres: single centre	Post-operative mortality and complications, Graft failure, patency at follow-up [Operative times based on presence or absence of intraoperative graft assessment via coronary angiography with iFR and pull back, not relevant to decision problem]	TTFM device used confirmed as VeriQ (Medistim) by corresponding author (02/03/2022) Not transparent how control group derived.
74.	Ucak 2020 Turkey	Cohort - retrospective (n=181) Intervention: coronary angiography and echocardiography before surgery	Patients with stable CAD who underwent elective CABG, under general anaesthesia and with cardiopulmonary bypass. Exclusion criteria: patients suffering with cardiac failure (systolic ejection fraction	Predictive factors of TTFM	Subgroup analysis by epicardial fat thickness (<5.5 mm, ≥5.5 mm)

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
		(measurement of epicardial fat thickness), VeriQ (Medistim) before skin closure. Comparator: N/A	<40%), BMI>40 kg/m^2, no optimal echocardiographic measurement. No. of centres: single centre (assumed from single affiliation of author)		
75.	Uehara *et al.* 2015 ~~ł~~Japan	Cohort (n=83) Intervention: BF1001 (Medistim); EAC assumes Butterfly device Comparator: coronary angiography (1 week) to determine: - Study 1: FitzGibbon grading (Grade A or Grade B/O) - Study 2: graft flow grade (good graft, bidirectional, occlusion including string)	Patients undergoing off-pump CABG with GEA grafts for RCA bypass. Patients with TTFM parameters and graft-flow waveforms recorded intraoperatively, stable vital signs, without catecholamines during the peri-operative period, and angiogram after 1 week were included. Study dates not reported. Exclusion criteria: not reported No. of centres: single centre~~ł~~	Correlation between early quality of graft and intraoperative TTFM values.	
76.	Une *et al.* 2013 Canada	Imaging subgroup from the "Graft Imaging to Improve Patency" GRIIP RCT (n=44) Intervention: TTFM (Medistim; device not reported)	Patients undergoing isolated, primary CABG with or without bypass. Recruitment period between September 2005 and July 2008. Exclusion criteria: LVEF <20%, contraindications to receiving intraoperative ICG dye or follow-up angiography (iodine allergy, severe liver	Graft occlusion (at 1 year angiography), MACCE (death, MI or repeat vascularisation)	Study population already reported in Singh *et al.* 2010 (included in original assessment report)

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
		Comparator: coronary angiography or multi-slice CT angiography (1 year)	disease affecting ICG excretion, chronic renal insufficiency: creatinine >180 mol/L, severe peripheral vascular disease, coagulopathy, obligatory use of anticoagulants, or geographically inaccessible to follow-up. Revised grafts and grafts without TTFM were also excluded. No. of centres: single centre		Conducts analysis to determine whether intraoperative TTFM is predictive of failure (including ROC analysis)
77.	Urbanowicz *et al.* 2021 [Pre-print, not peer reviewed] Poland	Cohort – retrospective (n=50) Intervention: Verify Q (*assumed by EAC to be VeriQ*), ECG on admission to ICU (immediately after procedure, then daily) Comparator: N/A	Consecutive patients who underwent off-pump CABG. Patients qualified for surgery based on coronary angiography results. All procedures performed via complete median sternotomy on the beating heart, without cardiopulmonary bypass support. Recruitment period: 2018 Exclusion criteria: not reported No. of centres: single centre	Peri-operative events (deaths, MI), long-term events (mean 897 days)	Subgroup analysis: obese (>30kg/m^2) and non-obese
78.	Vechersky *et al.* 2019 Russia	Cohort – prospective (n=68) Intervention: VeriQ (Medistim) used intraoperatively. Comparator: N/A	Patients who underwent CABG with no concomitant procedures. Patients with CAD, severe non-occluded coronary artery stenosis (70-90%), and the same body surface area (within 0.1 m^2 of 1.92 m^2). All CABG procedures performed through median sternotomy, with cardiopulmonary bypass. Recruitment in 2019. Exclusion criteria: concomitant cardiac procedures associated with CABG,	Graft failure, graft revision	Three measurements of TTFM made intraoperatively: - 1^{st} on cross clamp (with and without snare),

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
			emergency CABG, redo CABG, peripheral vascular disease, diabetes. No. of centres: single centre		- 2nd off-pump - 3rd before chest closure
79.	Vrancic *et al.* 2017 Argentina	Cohort – retrospective (n=3,118) Intervention: Exclusive bilateral ITA grafting, VeriQ (Medistim) Comparator: Single ITA, plus RA or AVG grafting, VeriQ (Medistim)	Consecutive patients with multi-vessel disease undergoing isolated CABG. Indications for myocardial revascularisation were based on standard clinical and angiographic criteria. All the patients were operated on through a median sternotomy. Recruitment period between January 2003 and September 2015. Exclusion criteria: not reported No. of centres: single centre	Post-operative events: mediastinitis, mortality, prolonged mechanical ventilation, stroke, redo for bleeding.	Includes propensity matching. Potential overlap with Vrancic *et al.* 2019
80.	Vrancic *et al.* 2019 Argentina	Cohort – retrospective (n=4,406) Intervention: VeriQ (Medistim) Comparator: N/A	Consecutive patients undergoing isolated CABG. Indications for myocardial revascularisation were based on standard clinical and angiographic criteria. All procedures were through median sternotomy. Recruitment period between January 2000 and April 2017. Exclusion criteria: not reported No. of centres: single centre	Early outcomes (30 days: mortality, stroke, mediastinitis, AF, MI, dialysis, reoperation for bleeding), long-term survival (10 years).	Subgroup analysis: by BITA/SITA and by gender Includes propensity matching. Potential overlap with Vrancic *et al.* 2017

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
81.	Yamamoto *et al.* 2017 Japan	Cohort - retrospective (n=69) Intervention: Indocynanine green angiography HEMS, coronary angiography (post-operatively), myocardial scintigraphy (10 days, in patients without coronary angiography), coronary angiography (1 year, unless myocardial ischaemia present) Comparator: VeriQ (Medistim)	Patients undergoing CABG, off-pump unless the patient's condition was critical, as in cardiogenic shock. Study dates not reported. Exclusion criteria: not reported No. of centres: Single centre	Measurement accuracy (comparison of mean graft flow, PI and diastolic filling compared for patent and failed grafts, as determined by angiography; Table 4).	Subgroup analysis by ITA and SVG/RA grafts.
82.	Yamamoto *et al.* 2022 ŧJapan	Cohort – retrospective (n=43) Intervention: High-resolution near-infrared angiography Comparator: VeriQ (Medistim), coronary or CT angiography (1 month)	Patients undergoing CABG, where the graft was assessed with high-resolution near-infrared angiography. Patients included had either unstable angina pectoris, effort angina pectoris, non-STEMI, old MI before surgery between 2016 and 2019. Off-pump CABG was performed unless the patient's condition was critical, such as in cases with cardiogenic status. Exclusion criteria: free grafts including ITA and SVG and RA anastomosed to the circumflex and RCA	Measurement accuracy	

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
			No. of centres: not reported		
83.	Yuan *et al.* 2018 China	Cohort – retrospective (n=508) Intervention: VeriQ (Medistim), coronary or CT angiography (n=112) Comparator: N/A	Patients with CAD undergoing total arterial off-pump CABG. The pre- and post-operative strategy and grafting approach were not altered throughout the entire study period. Recruitment between January 2007 and May 2017. Exclusion criteria: patients who underwent concomitant cardiac or aortic surgical procedure such as a valve replacement, valvuloplasty, or replacement of a valvular prosthesis. No. of centres: NR (single surgeon)	Early outcomes, during hospitalisation and within 30 days (mortality, LoS, bleeding requiring re-exploration, stroke, sternal infection, need for surgical debridement, sternal refixation). Follow-up (death, repeat revascularisation)	Graft patency not assessed in all patients.
84.	Zhang *et al.* 2020 China	Cohort – retrospective (n=410) Intervention: VeriQ (Medistim) intraoperatively, CT angiography prior to discharge (unless grade 3 or higher chronic kidney disease).	Patients undergoing isolated off-pump CABG, through median full sternotomy. Recruitment period between 1 October 2017 and 31 October 2019. Exclusion criteria: patients undergoing redo surgery, concomitant procedures, on-pump CABG, lacking intraoperative TTFM data. No. of centres: single centre	Graft patency, differences in flow between graft types	Subgrouped by graft type: LIMA (n=333), RIMA (n=34), and SVG (n=43). Measurement of preoperative (Doppler) flow and intraoperative graft flow (TTFM). Potential overlap with Mao *et al.*

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
		Comparator: Transthoracic doppler ultrasound pre-operatively			2020; unconfirmed.
85.	Zhang *et al.* 2021 China	Cohort – retrospective (n=360) Intervention: VeriQ (Medistim), multi-slice CT angiography prior to discharge Comparator: N/A	Patients undergoing primary isolated CABG with TTFM and CT angiography. All patients underwent CABG through median sternotomy. Recruitment period between October 2017 and December 2019. Exclusion criteria: sequential anastomoses, radial grafts, composite grafts. No. of centres: single centre	Graft failure (by type of graft), exploration of risk factors of graft failure	Potential overlap with Zhang *et al.* 2020 and Mao *et al.* 2020; unconfirmed. Subgroup analysis: - off-pump, on-pump - arterial and venous grafts - left and right territories
86.	Zhao *et al.* 2020a China	Cohort (n=242) Intervention: VQ2011 (EAC assumes this is VeriQ), CT angiography 1 week after surgery.	Patients undergoing simple CABG, with right coronary system for grafting. All patients underwent routine mid-opening, under cardiohepatic cardiopulmonary bypass or non-stop jumping. Recruitment period between October 2016 and March 2019. Exclusion criteria: patients with minimally invasive small incision, single or multiple grafts, patients who did not undergo TTFM during operation, patients who did not undergo CT at 1 week after surgery.	Graft failure and flow measurement (by bypass method)	Subgroup analysis by bypass method: - single bypass, - right crown sequential group, - sequential group with other systems

#	Author (year) and location	Design and intervention(s)	Participants and setting	Outcomes within scope	EAC comments
			No. of centres: single centre		Potential overlap with Zhang *et al.* 2021, Zhang *et al.* 2020, Mao *et al.* 2020
87.	Zhao *et al.* 2020b China	Cohort – retrospective (n=374) Intervention: VeriQ (Medistim), CT angiography (prior to discharge) Comparator: N/A	Patients undergoing isolated CABG. Recruitment between 1 October 2017 and 31 October 2019. Median full sternotomy used in most patients. Exclusion criteria: patients undergoing redo surgery, concomitant procedures, on-pump CABG, lacking intraoperative TTFM data, patients receiving RIMA to LAD revascularisation. No. of centres: single centre	Patency, graft revision	Subgroup by LIMA to LAD (n=332) and SVG to LAD (n=42). Included propensity matching.

Abbreviations: BIMA, bilateral internal mammary artery; BITA, bilateral internal thoracic artery; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CFVR, coronary flow velocity reserve; CT computed tomography; EAC, External Assessment Centre; ECMO, extracorporeal membrane oxygenation; EUS, epicardial ultrasonography; GEA, gastroepiploic artery; HEMS, HyperEye Medical System; FFT, fast Fourier transform IABP, intra-aortic balloon pump; LIMA, left internal mammary artery; LVEF left ventricular ejection fraction; MF, mean flow; MI, myocardial infarction; OM, obtuse marginal; RCA, right coronary artery; RITA, right internal thoracic artery; SITA, single internal thoracic arteries; TTFM, transit time flowmetry
*published before 2016 and not considered within previous guidance review
†Available in abstract only
ǂ Not explicitly stated, assumed from author affiliations

Appendix D4 – Narrative summary of included evidence

Of the 87 studies deemed in scope by the EAC, the study designs were as follows:

- nine RCTs, in which TTFM was used in both arms rather than as the intervention or comparator:
    - Erdem *et al.* (2015) compared impact of diltiazem infusion (intervention: with, comparator: without);
    - Tang *et al.* (2021) compared aspirin and tricagelor medication versus aspirin and clopidogrel;
    - Jiang *et al.* (2020) compared “no touch” SVG conduit technique and conventional technique;
    - Dreifaldt *et al.* (2013) included patients where each was assigned to receive one no-touch SVG and one radial artery (RA) graft to either the left (n=52) or right (n=48) coronary territory;
    - Satdhabudha *et al.* (2017) included patients undergoing coronary artery bypass grafting for left anterior descending artery (LAD) revascularization randomised to having semi skeletonised or conventional pedicled ITA graft harvested;
    - Pettersen *et al.* (2017) included patients undergoing pedicled or conventional vein harvesting;
    - Tamim *et al.* (2020) included patients undergoing endoscopic or open RA harvest technique;
    - Chang *et al.* (2018) compared revascularisation using a lower leg or upper leg saphenous vein (SV) composite graft on the in situ left ITA;

    - Ozdemir *et al.* (2019) compared CABG using RA, where the harvested RA was topically treated with verapamil (n=65) and where patients were treated with nicardipine (n=66);

- two subgroups of patients from an RCT:

    - Amin *et al.* (2018a): which included patients receiving external stenting of a single SVG randomly allocated intraoperatively to either left or right coronary territory, however all 35 included patients had flow measurements using the VeriQC device (no comparison made to angiography or intravascular ultrasound).

    - Une *et al.* (2012): included the imaging arm of the "Graft Imaging to Improve Patency (GRIIP)" RCT, where CABG grafts were assessed using fluorescence angiography and TTFM.

- 72 cohort studies (Acipayam *et al.* 2015; Amin *et al.* 2019; Amin *et al.* 2018b; An *et al.* 2019; Bazylev *et al.* 2018; Benetti *et al.* 2021; Borowski *et al.* 2017; Cerqueira Neto *et al.* 2012; Choi *et al.* 2021; Davierwala *et al.* 2021a; Davierwala *et al.* 2021b; Dayan *et al.* 2018; De Leon *et al.* 2020; Gao *et al.* 2021; Gestrich *et al.* 2020; Girish *et al.* 2019; Guo *et al.* 2019; Han *et al.* 2021; Handa *et al.* 2016; Harahsheh *et al.* 2012; Hashim *et al.* 2018; Hellmann *et al.* 2020; Hiraoka *et al.* 2017; Honda *et al.* 2015; Honda *et al.* 2019a; Honda *et al.* 2019b; Hosono *et al.* 2020; Hwang *et al.* 2018; Inderbitzin *et al.* 2015; Joshi *et al.* 2020; Kaya *et al.* 2018; Kim *et al.* 2020a; Kim *et al.* 2021; Kornovski *et al.* 2017; Kuroyanagi *et al.* 2012; Laali *et al.* 2021; Lee *et al.* 2020; Li *et al.* 2021a; Li *et al.* 2021b; Lobo *et al.* 2016; Mahmoud *et al.* 2017; Martinovic *et al.* 2019; Mohamed *et al.* 2019; Monsefi *et al.* 2016; Nakajima *et al.* 2016; Nakajima *et al.* 2018; Nakajima *et al.* 2019; Nakamura *et al.* 2019; Navia *et al.* 2016; Niclauss *et al.* 2020; Oshima *et al.* 2016; Rasekh & Mahmoud 2021; Reineke *et al.* 2012; Rufa *et al.* 2020; Sakabe *et al.* 2020; Seetharama Bhat *et al.* 2019; Sharipov *et al.* 2017; Shehada *et al.* 2019; Stastny *et al.* 2021; Tamura *et al.* 2021; Tolegenuly *et al.* 2020; Ucak 2020; Uehara *et al.* 2015; Urbanowicz *et*

al. 2021; Vechersky *et al.* 2019; Yamamoto *et al.* 2017; Yamamoto *et al.* 2022; Yuan *et al.* 2018; Zhang *et al.* 2020; Zhang *et al.* 2021; Zhao *et al.* 2021; Zhao *et al.* 2020a);

- one cohort study with control group (Tolegenuly *et al.* 2021) determining impact of intraoperative angiography, but where TTFM was recorded in all grafts;
- six cohort studies included propensity matched analysis:
    - bilateral internal thoracic artery (BITA) compared with SITA (Navia *et al.* 2016; Vrancic *et al.* 2017; Vrancic *et al.* 2019);
    - LIMA-LAD compared with SVG-LAD (Zhao *et al.* 2020b);
    - lower distal mini sternotomy off-pump CABG compared with standard off-pump CABG (Su *et al.* 2018);
    - off-pump compared with on-pump (Rufa *et al.* 2020).

Comparative evidence included:

- two quantitative assessment of graft flow (Amin *et al.* 2018b; Girish *et al.* 2019: free-flow measurement, however one expert has confirmed that qualitative free flow is the standard of care in the NHS not quantitative as reported in this study);
- one intraoperative and follow-up colour Doppler ultrasonography (at five to eight days follow-up: Gao *et al.* 2021);
- one intraoperative laser Doppler flowmetry (LDF) (Hellmann *et al.* 2020);
- one postoperative fluoroscopic coronary angiography (Yamamoto *et al.* 2017);

- seven studies used coronary angiography (intraoperatively: Tolegenuly *et al.* 2020; one week: Uehara *et al.* 2015; follow-up: Borowski *et al.* 2017; Oshima *et al.* 2016; Nakajima *et al.* 2019; Handa *et al.* 2016);
- one dynamic CT angiography (Sakabe *et al.* 2020);
- two multi-slice CT angiography before discharge (Hiraoka *et al.* 2017; Zhang *et al.* 2021);
- three studies used a mixture of coronary and CT angiography (one week: Kuroyanagi *et al.* 2012; one month: Yamamoto *et al.* 2022), and one mixture of coronary and multi-slice CT angiography (Une *et al.* 2012);
- one MRI phase-contrast measurement of flow (Reineke *et al.* 2012).

Three additional studies used TTFM as the comparator representing standard of care, with the intervention of interest being pre- and post-operative transoesophageal echocardiography (TEE) (Joshi *et al.* 2020), quantitative ICG via the HyperEye Medical System (HEMS) (Yamamoto *et al.* 2017) and high-resolution near-infrared angiography (Yamamoto *et al.* 2022).

The majority of studies also included other imaging techniques alongside TTFM but did not undertake any comparison of results with VeriQ or MiraQ:

- intraoperative graft-flow waveforms (Uehara *et al.* 2015);
- intraoperative fluorescence imaging (IFI) with idocyanine green (Honda *et al.* 2015; Honda *et al.* 2019a; Kuroyanagi *et al.* 2012);
- TEE intraoperatively (Mahmoud *et al.* 2017); before and after grafting (Joshi *et al.* 2020), or at one month (Su *et al.* 2018), three months (Guo *et al.* 2019); echocardiogram pre-operatively and at follow-up (Mahmoud *et al.* 2017); electrocardiogram (Urbanowicz *et al.* 2021); electrocardiogram and echocardiogram at multiple timepoints (Lim *et al.* 2021a; Martinovic *et al.* 2019); transthoracic echocardiogram at follow-up (Tamim *et al.* 2020);

- intra-graft Doppler-guidewire at one year (Hwang *et al.* 2018);

- intraoperative coronary angiogram (Davierwala *et al.* 2021b; Tolegenuly *et al.* 2021), or post-operatively (Nakajima *et al.* 2018; Rasekh & Mahmoud 2021) or early (one day: Kim *et al.* 2021, 2 weeks: Nakajima *et al.* 2016; Sakabe *et al.* 2020; undefined time point Choi *et al.* 2021; Tamura *et al.* 2021) or at follow-up (six months: Pettersen *et al.* 2017; 1 year: Chang *et al.* 2018; Honda *et al.* 2019a; Nakamura *et al.* 2019; three years - Bazylev *et al.* 2018; Dreifaldt *et al.* 2013; undefined time point at follow-up – Navia *et al.* 2016);

- CT angiography on completion (Nakajima *et al.* 2018), before discharge (Zhang *et al.* 2020; Zhao *et al.* 2020b), early (within 7 days: Kim *et al.* 2020a; Zhao *et al.* 2020a, 14 days: Nakajima *et al.* 2016, 3 months (Guo *et al.* 2019) or at follow-up (1 year: An *et al.* 2019; Handa *et al.* 2016, Inderbitzin *et al.* 2015);

- multi-slice CT angiography after CABG (Tolegenuly *et al.* 2020; Tolegenuly *et al.* 2021), before discharge (Jiang *et al.* 2020), or at one year (Honda *et al.* 2019a; Honda *et al.* 2019b; Li *et al.* 2021a; Tamim *et al.* 2020; Tang *et al.* 2021);

- combination of angiography types:

    - coronary or CT angiography prior to discharge (Davierwala *et al.* 2021a), post-operatively – time point not reported (Hosono *et al.* 2020) or follow-up (Lim *et al.* 2021b; Mohamed *et al.* 2019; Yuan *et al.* 2018);

    - coronary or multi-slice CT angiography at follow-up (Honda *et al.* 2015; Hwang *et al.* 2018; Shehada *et al.* 2019);

    - coronary angiography or multi-slice computed tomography (Monsefi *et al.* 2016);

    - cardiac catheterisation - which the EAC assumes may include angiography but type not described (Lim *et al.* 2021b).

- cardiac MRI at follow-up (6 to 12 weeks: Niclauss *et al.* 2020, approx. 1 year: Honda *et al.* 2019a; Honda *et al.* 2019b).

The included studies included a range of additional statistical analysis including TTFM:

- one study reported TTFM before and after graft revision (Seetharama Bhat *et al.* 2019);
- one study reported TTFM before and after valvulotomy through side branch (Monsefi *et al.* 2016);
- one study reported TTFM before and after clamping by graft type (Hosono *et al.* 2020);
- two studies performed receiver-operator characteristics curve analysis to determine the threshold of mean graft flow as a predictor of graft failure: perioperatively (Kaya *et al.* 2018), and at one year (Une *et al.* 2012);
- one study compared preoperative flow via Doppler ultrasound with intraoperative flow measured by VeriQ (Zhang *et al.* 2020);
- one study compared multiple TTFM measurements at different CABG time points (measured at cross-clamp before and after proximal snare, off-pump and before chest closure) (Vechersky *et al.* 2019);
- one study compared TTFM intraoperatively with preoperative left ventricular mass measured preoperatively via echo (Honda *et al.* 2019a);
- three studies aimed to determine whether TTFM intraoperatively or at completion of CABG were predictive of outcomes at follow-up (De Leon *et al.* 2020; Handa *et al.* 2016; Une *et al.* 2012);

- one study evaluated the correlation between TTFM and preoperative diameter of the recipient artery as measured with coronary angiography(at least 3 months prior to surgery (Borowski et al. 2017);
- one study aimed to determine if intraoperative TTFM was univariately or multivariately associated with conduit diameter at one year (Hwang *et al.* 2018);
- one study between intraoperative TTFM and pre-operative Rentrop collateral grade (Oshima *et al.* 2016);
- one study between final flow or flow with an arrested heart and pulsatility index (PI) (without bypass), diameter of target vessel, degree of stenosis, percentage of flow change and area of blood distribution (Stastny *et al.* 2021);
- one study aimed to determine if pre-operative and patient characteristics (age, hypertension, dyslipidaemia, high-sensitivity C-reactive protein, BMI, diabetes, epicardial fat thickness) were predictive of mean graft flow (Ucak 2020).

The majority of studies were single-arm (with no comparators). A variety of subgroup analyses were described, including:

- date of CABG procedure (Davierwala *et al.* 2020b) including pre- or post-introduction of TTFM (Kim *et al.* 2020a);
- on-pump and off-pump CABG (Amin *et al.* 2019; Cerqueira Neto *et al.* 2012; De Leon *et al.* 2020; Kornovski *et al.* 2017; Mahmoud *et al.* 2017; Rufa *et al.* 2020; Zhang *et al.* 2021);
- bypass method:
    - single and sequential grafts (Hosono *et al.* 2020),
    - single, double sequential, or triple sequential grafts (Dreidfaldt *et al.* 2013);

    - sequential grafts and Y-grafts (Acipayam *et al.* 2015);
    - single bypass, right crown sequential, sequential group with other systems (Zhao *et al.* 2020a);
- type of graft and graft configuration:
    - saphenous vein graft (SVG) and arterial grafts (Amin *et al.* 2019; Zhang *et al.* 2021),
    - SVG or gastroepiploic artery (GEA) grafts (Nakajima *et al.* 2019);
    - left or right internal mammary artery (LIMA, RIMA) and SVG (Zhang *et al.* 2020);
    - left anterior descending artery (LAD), circumflex coronary artery or RCA (Harahsheh *et al.* 2012),
    - right coronary artery (RCA), right circumflex artery (RCX), diagonal artery, marginal artery, LIMA-LAD (Reineke *et al.* 2012),
    - obtuse marginal (OM), posterior descending artery (PDA), LAD (De Leon *et al.* 2020);
    - distal internal thoracic artery (ITA), proximal ITA and SVG (Hwang *et al.* 2018);
    - ITA compared to SV or radial artery (RA) (Yamamoto *et al.* 2017);
    - LIMA, RIMA, RA and right gastroepiploic artery (RGEA) (Yuan *et al.* 2018);
    - LIMA-LAD and SVG-LAD (Zhao *et al.* 2020b);
    - different locations of anastomoses and different coronary systems (Li *et al.* 2021a);

    - bilateral internal thoracic artery (BITA) grafting and single internal thoracic artery (SITA) grafting; including further subgroups of patients who underwent operation with left internal thoracic artery (LITA) and RA without or without SVG, and those receiving LITA supplemented by SVG only (Navia *et al.* 2016);
    - left and right territory (Amin *et al.* 2018a; Zhang *et al.* 2021),
    - LIMA and RIMA (Stastny *et al.* 2021),
    - grafting of the right internal mammary artery (RIMA) to bilateral or left target territories (Han *et al.* 2021),
    - left side arterial graft, right and left sided vein grafts (Hiraoka *et al.* 2017);
- stented and non-stented grafts (Amin *et al.* 2018a);
- endoscopic or open approach in saphenous vein harvesting (Tamura *et al.* 2021);
- number of grafts (Borowski *et al.* 2017);
- number of donor sources (Borowski *et al.* 2017);
- diameter of target vessels, dichotomised as less than 1.5 mm and greater or equal to 1.5 mm (An *et al.* 2019; Niclauss *et al.* 2020);
- patients in whom ligation of the anterior descending artery (ADA) was performed, and those not (Bazylev *et al.* 2018);
- collateral filling from the contralateral vessel by the Rentrop grade (Borowski *et al.* 2017; Gestrich *et al.* 2020);
- ipsilateral collateral connection (Borowski *et al.* 2017);
- pre-operative severity of coronary artery stenosis:

    - fractional flow reserve (categorised as severe, mild, functionally no stenosis) (Honda *et al.* 2015)
    - stenosis determine by angiography (binary: less than 90%, greater than or equal to 90%) (Niclauss *et al.* 2020);
    - instantaneous wave-free ratio (iFR) categorised into three groups: less than 0.86, 0.86-0.90, greater than 0.90 (Tolegenuly *et al.* 2020);
- epicardial fat thickness (binary: less than 5.5 mm, greater than or equal to 5.5 mm) (Ucak 2020);
- native coronary flow (binary: less than or equal to 1, greater than 1) (Niclauss *et al.* 2020);
- pulsatility index (PI less than or equal to 3, PI greater than 3) (Joshi *et al.* 2020);
- with and without left main coronary artery disease (Sharipov *et al.* 2017);
- with and without IABP (Nakajima *et al.* 2016; Nakamura *et al.* 2019);
- comorbidities:
    - including hypoakinesia, Q-infarction, diabetes, hyperlipidaemia (Borowski *et al.* 2017);
    - with and without left ventricular hypertrophy (Honda *et al.* 2019a);
    - patients undergoing haemodialysis and those not (Honda *et al.* 2019b);
    - obesity based on BMI (Urbanowicz *et al.* 2021);
    - prior history of percutaneous coronary intervention (PCI); binary (Nakajima *et al.* 2018);

- age (younger than 60, 60 to 75 years; Guo *et al.* 2019);
- gender (Vrancic *et al.* 2019);
- with and without pre-operative beta-blockers (Dayan *et al.* 2018);
- patients undergoing off-pump CABG with coronary endartectomy with and without distal anastomosis support (DAS) (Lim *et al.* 2021b);
- lower distal mini-sternotomy off-pump CABG and standard full length-sternotomy off-pump CABG (Su *et al.* 2018).

Appendix D5 – Tabulated summary of included studies by outcome

						Outcomes								
Author (year)	Study design	No. of patients	Description of graft (number, type, and location, as available)	Intervention	Comparator	Graft failure	Time to graft failure	Peri- and post-operative clinical events associated with graft failure	Need for graft revision	Long-term morbidity and mortality	Measurement accuracy	Time taken to generate and record data during operation	No. probes used	No. times each probe used
Erdem *et al.* 2015	RCT	140	361 (included 135 LIMA, 156 SVG, 70 RA)	CABG + diltiazem infusion + VeriQ	CABG + VeriQ			✓	✓					
Chang *et al.* 2018	RCT	26	26 (26 Y-composite grafts based on LITA)	Graft using upper leg vein; TTFM with Medistim device, and coronary angiography (1.1 days and 1 year)	Graft using lower leg vein; TTFM with Medistim device, and coronary angiography (1.1 days and 1 year)	✓								
Dreifaldt *et al.* 2013	RCT	108	198 (99 no-touch SVG, 99 RA)	Graft to right coronary territory, VeriQ, coronary angiography (3 years)	Graft to left coronary territory, VeriQ, coronary angiography (3 years)	✓		✓	✓	✓				
Jiang *et al.* 2020	RCT	59	NR (LIMA to LAD, and sequential SVG to three non-LAD targets)	"no touch" harvest technique (TTFM with VeriQ + multi-slice CT angiography)	Standard harvest technique (TTFM with VeriQ + multi-slice CT angiography)	✓		✓	✓					
Ozdemir *et al.* 2019	RCT	131	NR	Verapamil + VeriQ	Nicardipinen + VeriQ			✓		✓				
Pettersen *et al.* 2017	RCT	100	All LIMA to LAD, with SVG used for further revascularisation	Pedicled vein harvesting + VeriQ	Conventional vein harvesting + VeriQ	✓		✓	✓					
Tamim *et al.* 2020	RCT	50	3 RA to diagonal, 21 RA to obtuse marginal (OM), 9 RA to ramus, 12 RA to RCA, 5 RA to PDA, 50 LIMA to LAD, 4 LIMA to diagonal, 3 RIMA to diagonal, 2 RIMA to OM, 6 RIMA to RCA, 11 SVG to diagonal, 19 RIMA to OM, 4 SVG to ramus, 20 SVG to RCA, 21 SVG to PDA	Endoscopic RA harvest, TTFM (Medistim; device not reported), multi-slice CT angiography (1 year), transthoracic echo (1 year), 12 lead ECG (1 year)	Open RA harvest, TTFM (Medistim; device not reported), multi-slice CT angiography (1 year), transthoracic echo (1 year), 12 lead ECG (1 year)	✓		✓		✓				
Tang *et al.* 2021	RCT	147	517 (144 LIMA, 336 SVG, 37 sequential)	aspirin+tricagelor, TTFM by Medistim device	aspirin+clopidogrel, TTFM by Medistim device	✓		✓		✓				
Satdhabudha *et al.* 2017	RCT	60	60 (LITA to LAD)	Semiskeletonised (flow measured by VeriQ)	Pedicled (flow measured by VeriQ)			✓						
Une *et al.* 2013	Cohort - subgroup of RCT (imaging arm)	44	106 (41 arterial, 65 SVG)	TTFM (Medistim; device not reported)	Coronary or CT angiography (1 year)	✓				✓				
Gao *et al.* 2021	Cohort	52	NR (52 in situ LIMA to LAD, some patients had additional arterial grafts or SVG)	CardioMed Trace System (predated VeriQ/MiraQ)	Colour doppler ultrasound (pre-op, 5 to 8 days after surgery)			✓	✓					
Girish Gowda *et al.* 2019	Cohort	NR	48 SVG	VeriQ	Free-flow (blood collected for 15 seconds)						✓			
Uehara *et al.* 2015	Cohort	83	83	BF1001	Coronary angiography (1 week)									
Joshi *et al.* 2020	Cohort (prospective)	40	120 (40 arterial LIMA to LAD, 80 right SVG to OM or right coronary artery (RCA)).	TEE	VeriQ				✓					
Sakabe *et al.* 2020	Cohort (prospective)	14	26 (11 ITA, 15 SVG)	VeriQ	Dynamic cardiac CT with CT angiography obtained as boost scan (2 weeks) and visually evaluated.									
Tolegenuly *et al.* 2020	Cohort (prospective)	25	89 (25 arterial, 64 vein grafts)	VeriQC, coronary angiography	iFR (coronary angiography)	✓		✓	✓					
Hellmann *et al.* 2020	Cohort (prospective)	26	54 (15 LIMA to LAD, 10 RIMA to LAD 9 LIMA to marginal branch, 5 LIMA to diagonal branch, 1 RIMA to marginal branch, 5 SVG to marginal branch, 4 SVG to intermediate artery, 2 SVG to diagonal branch, 1 SVG to posterior descending artery (PDA), 1 to posterolateral branch of circumflex artery, 1 SVG to posterolateral branch of RCA)	VeriQ	LDF						✓ǂ			
Reineke *et al.* 2012	Cohort (prospective)	27	56 (6 SVG to diagonal artery, 7 SVG to marginal artery, 1 SVG to LAD, 18 SVG to RCA, 7 SVG to right circumflex artery, 16 LIMA to LAD, 1 RIMA to RCA)	CardioMed	MRI phase contrast flow measurements (within 1 week)									

Author (year)	Study design	No. of patients	Description of graft (number, type, and location, as available)	Intervention	Comparator	Outcomes								
						Graft failure	Time to graft failure	Peri- and post-operative clinical events associated with graft failure	Need for graft revision	Long-term morbidity and mortality	Measurement accuracy	Time taken to generate and record data during operation	No. probes used	No. times each probe used
Tolegenuly *et al.* 2021	Cohort (prospective)	100	Used LIMA to LAD, and SVGs to right coronary or circumflex arteries (exact details not reported)	Coronary angiography with iFR and pullback (using pressure guide wire), VeriQ (Medistim confirmed by author), CT angiography (follow- up)	VeriQ (Medistim confirmed by author)	✓		✓	✓					
Vrancic *et al.* 2017	Cohort (retrospective: incl. propensity matching)	3,118	2,533 BITA, 585 SITA	Exclusive bilateral ITA grafting, VeriQ	Single ITA, plus RA or SVG grafting, VeriQ			✓						
Amin *et al.* 2018b	Cohort (retrospective)	60	60 (LIMA graft)	VeriQC	Free flow						✓			
Oshima *et al.* 2016	Cohort (retrospective)	196	214 (75 LITA to LAD, 3 LITA to left circumflex artery, 5 RITA to LAD, 3 RITA to left circumflex artery, 2 RITE to RCA, 14 RGEA to RCA, 2 SVG to LAD, 4 SVG to diagonal artery, 22 SVG to left circumflex artery, 84 SVG to RCA)	VeriQ	Coronary angiography (1 month), Retrop grading of collateral filling (pre-operatively)	✓								
Handa *et al.* 2016	Cohort (retrospective)	68	114 (all aortocoronary artery)	VeriQ	Coronary angiography (at 1 year)	✓				✓†				
Su *et al.* 2018	Cohort (retrospective)	288	907 (288 LITA to LAD, 331 SVG or RA to LCX, 288 SVG to RCA)	Lower distal mini-sternotomy off-pump CABG, TTFM by Medistim device	Off-pump CABG, TTFM by Medistim device			✓	✓	✓				
Zhang *et al.* 2020	Cohort (retrospective)	410	410 (333 LIMA to LAD, 34 RIMA to LAD, 43 SVG to LAD)	VeriQ	Doppler ultrasound (pre-operatively)	✓								
Borowski *et al.* 2017	Cohort (retrospective)	69	69 (65 venous, 4 in situ RITA)	VeriQ	Coronary angiography (CTO estimated over 3 months pre-operatively)					✓				
Hiraoka *et al.* 2017	Cohort (retrospective)	63	104 (59 LITA, 12 RITA, 33 SVG)	VeriQ	CT angiography (prior to discharge)	✓		✓	✓					
Honda *et al.* 2019a	Cohort (retrospective)	155	155 (155 in situ ITA to LAD)	VeriQ, fluorescence imaging	Echocardiography (pre-op)					✓				
Honda *et al.* 2019b	Cohort (retrospective)	161	161 (161 in situ ITA to LAD)	VeriQ, fluorescence imaging	Pre- and post-operative echocardiography					✓				
Laali *et al.* 2021	Cohort (retrospective)	925	Arterial revascularisation with single or bilateral ITA, with Y-configuration (exact details not reported)	TTFM (Medistim; device not reported)	No TTFM			✓	✓			✓°		
Yamamoto *et al.* 2017	Cohort (retrospective)	69	177 (75 ITA, 13 RA, 89 SVG)	ICG angiography, coronary angiography (post-operatively), myocardial scintigraphy, coronary angiography (1 year)	VeriQ						✓†			
Yamamoto *et al.* 2022	Cohort (retrospective)	43	In situ ITA to LAD	VeriQ	Coronary angiography	✓								
Amin *et al.* 2018a	Cohort - subgroup from RCT	35	115 (42 arterial conduits, 35 stented SVGs, 38 non-stented SVGs)	VeriQC	N/A				✓					
Amin *et al.* 2019	Cohort	268	506 (336 arterial, 170 venous)	VeriQC	N/A				✓					
An *et al.* 2019	Cohort	212	212 (aortosequential SVG to non-left anterior descending targets, and the LIMA to the LAD	VeriQ, and CT angiography (at 1 year)	N/A	✓		✓		✓				
Choi *et al.* 2021	Cohort	1,043	2,096 (1,001 LITA, 968 SVG, 113 RITA, 13 RGEA, 1 RA)	TTFM (Medistim; device not reported), coronary angiography (post-operative early)	N/A			✓						
Hashim *et al.* 2018	Cohort	60	86 (LIMA/RIMA to OM/LAD/RAMUS/LCX/INTERMEDIATE/DIAGONAL)	VeriQ	N/A			✓	✓					
Inderbitzin *et al.* 2015	Cohort	22	50 (17 LIMA, 4 RIMA, 1 RA, SVG unmeshed: 3 right; 4 left, SVG meshed: 11 right; 10 left)	MiraQ, CT angiography (1 year follow-up)	N/A	✓		✓						
Kornovski *et al.* 2017	Cohort	64	161 (55 LIMA to LAD, 4 LIMA to diagonal, 1 LIMA to right circumflex, 36 RIMA to right circumflex, 11 RIMA to right circumflex, 12 RIMA to RCA, 6 RA and right circumflex + RCA, 15 SVG to right circumflex, 15 SVG to RCA, 5 SVG to diagonal, 1 SVG to LAD)	VeriQ	N/A	✓		✓						

Author (year)	Study design	No. of patients	Description of graft (number, type, and location, as available)	Intervention	Comparator	Outcomes								
						Graft failure	Time to graft failure	Peri- and post-operative clinical events associated with graft failure	Need for graft revision	Long-term morbidity and mortality	Measurement accuracy	Time taken to generate and record data during operation	No. probes used	No. times each probe used
Martinovic *et al.* 2019	Cohort	12	NR	VeriQC, electrocardiography (during admission), coronary angiographyechocardiography (pre, intraoperative, at discharge)	N/A			✓						
Monsefi *et al.* 2016	Cohort	147	592 (230 LIMA-anterior wall, 118 RIMA-Cx, 23 RA-Cx, 162 SVG-RCA, 59 SVG-Cx)	VeriQ, multi-slice CT, coronary angiography	N/A	✓		✓	✓					
Rasekh & Mahmoud 2021	Cohort	100	In situ LIMA to LAD, free RIMA to diagonal branch and OM branch, SVG to right coronary or its branches	VeriQ, echocardiography (post-operatively), coronary angiography	N/A			✓						
Seetharama Bhat *et al.* 2019	Cohort	424	1,203	VeriQ	N/A			✓	✓					
Stastny *et al.* 2021	Cohort	134	432 (including 134 LIMA, 57 RIMA, bilateral internal mammary artery (BIMA) grafts in 57 patients)	VeriQ	N/A	✓		✓						
Zhao *et al.* 2020a	Cohort	242	NR	VQ2011, CT angiography (1 week)	N/A	✓								
Harahsheh *et al.* 2012	Cohort (prospective)	436	1,394 (630 LAD, 425 circumflex coronary artery, 339 RCA)	VQ-1101	N/A	✓			✓					
Hwang *et al.* 2018	Cohort (prospective)	23	NR	TTFM (Medistim; device not reported), ultrasound, coronary or multi-slice CT angiography (1 year), intra-graft flow Doppler (1 year, n=6)	N/A	✓				✓				
Lee *et al.* 2020	Cohort (prospective)	57	163 (57 LIMA to LAD, 50 SVG to OMA, 35 PDA, 8 diagonal artery, 1 posterolateral artery, 6 ramus intermedius artery, 6 distal RCA)	VeriQ	N/A			✓						
Li *et al.* 2021a	Cohort (prospective)	259	518 (180 individual LIMA to LAD, 79 individual SVG to LAD, 259 sequential SVG: 235 to diagonal branch, 229 to OM branch, 62 to posterior left ventricular branch, 177 to PDA, 82 to RCA)	VeriQ, multi-slice CT angiography (1 year), electrocardiography and echocardiography (time point not defined)	N/A	✓		✓						
Lobo *et al.* 2016	Cohort (prospective)	23	46 (23 LITA to anterior interventricular artery, 7 SVG to diagonal branch of anterior interventricular artery, 3 SVG to diagonalis branch of left coronary artery (LCA), 13 SVG to marginal branch of circumflex artery)	Butterfly flowmeter (Medistim)	N/A			✓						
Mohamed *et al.* 2019	Cohort (prospective)	50	All radial (76% isolated: 9 to diagonal, 23 to OM, 6 to posterior descending or posterolateral branch of RCA, 24% sequential: 3 to OM and diagonal, 9 to OM)	VeriQC, CT angiography (n=8), coronary angiography (n=4)	N/A	✓		✓	✓	✓				
Nakamura *et al.* 2019	Cohort (prospective)	393	All LIMA to LAD, followed by grafting of circumflex coronary artery and RCA using RA or SVG.	VeriQ, coronary angiography, echocardiography, CT and MRI, single photon emission CT.	N/A			✓		✓				
Niclauss *et al.* 2020	Cohort (prospective)	35	99 distal anastomoses (35 to LAD, 12 to diagonal branches, 33 to circumflex/marginal branches, 19 to PDA/RCA)	VeriQC and QuickFit TTFM probe (Medistim), coronary angiography (timing not explicitly reported), cardiac MRI (6 to 12 weeks)	N/A			✓		✓				
Sharipov *et al.* 2017	Cohort (prospective)	270	LIMA or RIMA used in all patients	MiraQ	N/A			✓						
Vrancic *et al.* 2019	Cohort (retrospective: incl. propensity matching)	4,406	2,979 BITA, 627 SITA plus RA, 540 SITA plus RA and SVG, 260 SITA plus SVG	VeriQ	N/A			✓		✓				
Acipayam *et al.* 2015	Cohort (retrospective)	60	60 (36 sequential grafts, 24 Y-grafts)	VQ-1101	N/A			✓	✓					
Bazylev *et al.* 2018	Cohort (retrospective)	17	17 (ADA in connection with detected myocardial bridge, LITA used as conduit)	VeriQ, and coronary angiography (up to 3 years)	N/A	✓	*							
Benetti *et al.* 2021	Cohort (retrospective)	70	NR (LITA to LAD)	Medistim device	N/A	✓		✓	✓	✓				
Cerqueira Neto *et al.* 2012	Cohort (retrospective)	35	NR	Medistim (transducers and BF 2004 display)	N/A			✓	✓					

Author (year)	Study design	No. of patients	Description of graft (number, type, and location, as available)	Intervention	Comparator	Outcomes								
						Graft failure	Time to graft failure	Peri- and post-operative clinical events associated with graft failure	Need for graft revision	Long-term morbidity and mortality	Measurement accuracy	Time taken to generate and record data during operation	No. probes used	No. times each probe used
Davierwala *et al.* 2021a	Cohort (retrospective)	88	172 (87 to LAD artery territory, 76 to circumflex territory, 9 to RCA territory)	TTFM (Medistim; device not reported), coronary or CT angiography (assumed prior to discharge)	N/A	✓		✓	✓	✓				
Davierwala *et al.* 2021b	Cohort (retrospective)	2,667	NR (LITA to LAD, some additional grafts to diagonal branch; numbers not reported)	MiraQ, coronary angiography (assumed intraoperatively)	N/A			✓		✓				
Dayan *et al.* 2018	Cohort (retrospective)	282	NR (75 patients received more than 1 IMA graft)	VeriQ	N/A			✓		✓				
De Leon *et al.* 2020	Cohort (retrospective)	177	543 (248 arterial)	VeriQ	N/A			✓	✓	✓				
Gestrich *et al.* 2020	Cohort (retrospective)	404	NR (LIMA to LAD, venous graft to left circumflex artery dependent vessels, or RCA dependent vessels)	TTFM via QuickFit probe	N/A									
Guo *et al.* 2019	Cohort (retrospective)	155	303 (92 LIMA to OM, 44 LIMA to diagonal branch artery, 19 LIMA to LAD, 129 RIMA to LAD, 18 RIMA to OM, 8 RIMA to RCA)	VeriQ, and echocardiography and CT angiography (3 months)	N/A	✓		✓	✓	✓				
Han *et al.* 2021	Cohort (retrospective)	74	94 (20 patients BIMA, 54 LIMA)	VeriQ	N/A	✓		✓						
Honda *et al.* 2015	Cohort (retrospective)	72	72 (In situ ITA-to-LAD: 14 right; 58 left)	VeriQ, fluorescence imaging with ICG (intraoperatively), multi-slice CT angiography/MRI/coronary angiography (post-operatively within 1 year)	N/A	✓		✓	✓	✓				
Hosono *et al.* 2020	Cohort (retrospective)	24	108 (23 LITA to LAD, 1 LITA to diagonal, 17 RITA to diagonal, 18 RITA to OM, 4 RITA to posterolateral, 1 SVG to diagonal, 13 SVG to posterolateral, 3 SVG to right coronary, 19 SVG to posterior descending, 9 SVG to atrioventricular node)	Medistim (device not reported), coronary and multi-slice CT angiography	N/A	✓		✓						
Kaya *et al.* 2018	Cohort (retrospective)	1,240	3,596 (1,230 LIMA, 128 RA, 2,230 SVG, 8 cephalic vein graft)	VQ-1101 (Medistim), electrocardiography	N/A			✓	✓					
Kim *et al.* 2020a	Cohort (retrospective)	2,919	6,148 (2,764 LITA, 866 RITA, 997 RGEA, 16 RA, 1,505 SVG)	Off-pump CABG (Subgroup analysis by year, and by inclusion of TTFM by Medistim [device not reported])	N/A	✓		✓	✓	✓†				
Kim *et al.* 2021	Cohort (retrospective)	1,283	NR	TTFM (Medistim; device not reported), coronary angiography (mean 1.4 days, 1 year)	N/A	✓								
Kuroyanagi *et al.* 2012	Cohort (retrospective)	159	435 (142 RITA, 155 LITA, 88 GEA, 50 SVG)	VeriQC or Butterfly Flowmeter , indocynanine green (intraoperatively), coronary or CT angiography (approx. 1 week)	N/A	✓			✓					
Li *et al.* 2021b	Cohort (retrospective)	200	All LIMA, SVG	TTFM (Medistim; device not reported), CT angiography (6 months, 1 year, annually), coronary angiography	N/A	✓		✓		✓				
Mahmoud *et al.* 2017	Cohort (retrospective)	400	NR	TTFM (Medistim; device not reported), TEE (intraoperatively), echocardiography (pre- and post-operatively)	N/A			✓						
Nakajima *et al.* 2016	Cohort (retrospective)	32	76 (50 in situ grafts: 38 ITA, 3 gastroepiploic artery (GEA), 9 composite; 26 aortocoronary grafts: 25 SVG, 1 free ITA; total 102 distal anastomoses)	TTFM (Medistim; device not reported) and CT angiography or coronary angiography (approx. 2 weeks) in patients without renal dysfunction or other comorbidity.	N/A	✓								
Nakajima *et al.* 2018	Cohort (retrospective)	405	736 (334 in situ ITA to LAD, 129 in situ ITA to LCX, 65 SVG to LCX, 142 in situ GEA to RCA, 66 SVG to RCA)	TTFM (Medistim; device not reported) and postoperative coronary angiography (time point not defined)	N/A	✓								

Author (year)	Study design	No. of patients	Description of graft (number, type, and location, as available)	Intervention	Comparator	Outcomes								
						Graft failure	Time to graft failure	Peri- and post-operative clinical events associated with graft failure	Need for graft revision	Long-term morbidity and mortality	Measurement accuracy	Time taken to generate and record data during operation	No. probes used	No. times each probe used
Nakajima *et al.* 2019	Cohort (retrospective)	230	230 (155 in situ GEA, 75 aortocoronary SVGs)	TTFM (Medistim; device not reported), Coronary angiography (mean 1.5 months)	N/A	✓								
Navia *et al.* 2016	Cohort (retrospective)	3,757	2,098 BITA in T configuration, 1,659 SITA plus SVG or RA, or both	VeriQ, postoperative angiography (time point NR)	N/A			✓		✓				
Rufa *et al.* 2020	Cohort (retrospective)	304	135 LITA, 176 RITA, 38 RA, 172 SVG	VeriQ	N/A			✓	✓	✓				
Shehada *et al.* 2019	Cohort (retrospective)	112	474 grafts in total	TTFM (Medistim; device not reported), coronary or multi-slice CT angiography	N/A	✓		✓	✓	✓				
Tamura *et al.* 2021	Cohort (retrospective)	169	NR	VeriQ, coronary angiography (post-operatively within 14 days)	N/A	✓		✓						
Ucak 2020	Cohort (retrospective)	181	434 (162 LIMA to LAD, 19 SVG to LAD, 58 SVG to diagonal branches of LAD, 97 SVG to circumflex coronary artery, 98 SVG to RCA)	VeriQ	N/A									
Urbanowicz *et al.* 2021	Cohort (retrospective)	50	LIMA, RIMA, and left RA	Verify Q (assumed VeriQ), ECG	N/A			✓		✓				
Vechersky *et al.* 2019	Cohort (retrospective)	68	214 (LIMA used in all patients as a pedicled bypass graft, SVG used in all patients as aortocoronary grafts)	VeriQ	N/A				✓					
Yuan *et al.* 2018	Cohort (retrospective)	508	Standard LIMA-LAD anastomosis (n=507), LIMA dissection with RIMA-LAD anastomosis (n=1).	VeriQ, coronary or CT angiography	N/A	✓	*	✓	✓					
Zhang *et al.* 2021	Cohort (retrospective)	360	761 (364 arterial, 397 venous)	VeriQ, Multi-slice CT angiography (before discharge)	N/A	✓								
Zhao *et al.* 2020b	Cohort (retrospective)	374	Patients stratified by LAD revascularisation (LIMA, n=332; SCG, n=42)	VeriQ, CT angiography	N/A	✓		✓						

Abbreviations: ADA, anterior descending artery; BIMA, bilateral internal mammary artery; CABG, coronary artery bypass graft; CT, computed tomography; ECG, electrocardiogram; ; GEA, gastroepiploic artery; RGEA, right gastroepiploic artery; iFR, instantaneous wave-free ratio;; LAD, left anterior descending artery; LCX, left circumflex artery; LCA, Left coronary artery;LTA, left internal thoracic artery; OM, obtuse marginal; PDA, posterior descending artery; RA, radial artery; RAMUS, ramus coronary artery; SVG, saphenous vein graft; TEE, transesophageal echocardiography.
* Kaplan-Meier plot included in paper, however results at specified time intervals not explicitly reported.
† TTFM as predictive indicator of outcome at follow-up.
ǂ correlation of flow characteristics
° only time of procedure with and without TTFM reported

Appendix E – References

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