National Institute for Health and Care Excellence

Final

Abdominal aortic aneurysm: diagnosis and management

Evidence review N: Signs, symptoms and risk factors predicting ruptured or symptomatic unruptured aneurysms before arrival at the hospital, and in non-specialist hospital settings

NICE guideline NG156

Methods, evidence and recommendations

March 2020

Final

This evidence review was developed by the NICE Guideline Updates Team

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

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ISBN: 978-1-4731-3452-2

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Predicting ruptured or symptomatic aneurysms before arrival at the hospital, and in non-specialist hospital settings

Review question

Which signs, symptoms, risk factors (or combinations of these) and diagnostic assessment tools are most accurate in indicating the presence of a ruptured or symptomatic unruptured abdominal aortic aneurysm i) before arrival at the hospital and ii) in a non-specialist hospital setting?

Introduction

This review question aims to determine which signs, symptoms and risk factors:

- predict the presence of 'emergency' (that is, ruptured or symptomatic unruptured) abdominal aortic aneurysms
- would lead to immediate transfer to a specialist vascular unit (i.e. bypassing non-specialist A&E)
- should initiate definitive imaging in the emergency department (i.e. sufficient suspicion to initiate imaging, but not so high that a patient should be transferred to a vascular unit without imaging)

PICO

Table 1: Inclusion criteria

Parameter	Inclusion criteria
Population	• People with a suspected ruptured or symptomatic unruptured abdominal aortic aneurysm
Index test / factors of interest	• Pulsatile abdominal mass • Abdominal, back or groin pain • Sweating • Clamminess • Shock • Altered mental/cognitive status • Loss of consciousness • Collapse • Paralysis • Dizziness • Nausea • Vomiting • Hypotension • Fast pulse / tachycardia • Shortness of breath • Cyanosis

Parameter	Inclusion criteria
	• Urinary symptoms • Colic • Peripheral ischemia / absent peripheral pulses • Temperature • Capillary refill time • Ultrasound ('fast scan')
Endpoints	• Surgical or CT confirmation of rupture • CT confirmation of AAA accompanied by symptoms

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in Appendix A.

Declarations of interest were recorded according to NICE's 2014 conflicts of interest policy.

A broad search was used to identify all studies that examine the diagnosis, surveillance or monitoring of abdominal aortic aneurysms (AAA). This was a 'bulk' search covering multiple review questions. The database was sifted to identify all studies that met the criteria detailed in Table 1. The relevant review protocol can be found in Appendix A.

Studies were considered for inclusion if they were were cross-sectional studies or systematic reviews (of cross-sectional studies) exploring signs, symptoms or risk factors indicative of AAA rupture outside a regional vascular service setting.

Studies were excluded if they:

- were not in English
- were not full reports of the study (for example, published only as an abstract)
- were not peer-reviewed.

Clinical evidence

Included studies

From an initial database of 16,274 abstracts, 2 were identified as being potentially relevant. Following full-text review of these articles, no studies were included.

An update search was conducted in December 2017, to identify any relevant studies published during guideline development. The search found 2,180 abstracts; all of which were not considered relevant to this review question. As a result no additional studies were included.

Excluded studies

The list of papers excluded at full-text review, with reasons, is given in Appendix E.

Summary of clinical studies included in the evidence review

No studies were included following full text review.

Quality assessment of clinical studies included in the evidence review

No studies were included following full text review.

Economic evidence

Included studies

A literature search was conducted jointly for all review questions by applying standard health economic filters to a clinical search for AAA. This search returned a total of 5,173 citations. Following review of all titles and abstracts, no studies were identified as being potentially relevant to the review question. No full texts were retrieved, and no studies were included as economic evidence.

An update search was conducted in December 2017, to identify any relevant health economic analyses published during guideline development. The search found 814 abstracts; all of which were not considered relevant to this review question. As a result no additional studies were included.

Excluded studies

No studies were retrieved for full-text review.

Evidence statements

No evidence was identified for this review question.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The committee considered that the outcomes that matter most in non-specialist settings were symptoms and signs that, when considered in combination with risk factors, could be used as a strong indication of the presence of a ruptured aneurysm.

The quality of the evidence

The committee noted that there are currently no national criteria for predicting the presence of ruptured AAAs and the use of criteria varied according to local arrangements. In the absence of any evidence from prospective observational studies, the committee agreed that consensus recommendations were needed to ensure that clinicians in non-specialist settings are clear when a ruptured AAA should form part of a differential diagnosis.

Following discussion of the range of symptoms and risk factors presented in the review protocol the committee agreed that it would not be feasible to provide a comprehensive list of factors indicative of ruptured AAAs in non-specialist care settings. The committee also agreed that individual symptoms and signs are not usually used in isolation to predict the presence of ruptured aneurysms. As a result, the committee discussed key symptoms and signs that, when considered in combination with risk factors, would give the strongest indication of a ruptured aneurysm.

After considering the symptoms, signs and risk factors outlined in the review protocol, the committee agreed that a change in body temperature was not sensitive enough to predict the presence of a ruptured AAA in non-specialist care settings. Conversely, new abdominal and/or back pain, cardiovascular collapse and loss of consciousness were considered important symptoms indicative of a ruptured aneurysm. It was noted that the reliability of the aforementioned symptoms would be strengthened when observed in the presence of one or more significant risk factors.

In relation to risk factors, the committee agreed that people with a previously diagnosed asymptomatic AAA who present with any of the above-mentioned symptoms were most likely to have a ruptured aneurysm. Age was considered to be the second most important risk factor. The committee discussed various age thresholds, noting that the risk of AAA gradually increases with age but there is no published evidence of a specific age at which the risk of aneurysm rupture increases markedly. The committee agreed that ruptured AAAs were exceptionally rare in people younger than 60. Furthermore, they were in agreement that, in their experience, people over 60 were more likely to present at an A&E department with a ruptured AAA than people younger than 60. It was noted that the guideline recommendation aligns with the National AAA Screening Programme which does not offer screening to men until they reach 65.

Benefits and harms

The committee felt that defining a set of symptoms, signs and risk factors that are particularly indicative of a ruptured aneurysm, would highlight when clinicians in non-specialist settings would know when AAA should form part of a differential diagnosis. This would increase the chances of aneurysms being detected and therefore increase the likelihood of patient survival.

Cost effectiveness and resource use

The committee felt that the recommendations are unlikely to impact on costs and resource use, as they were informative in nature.

Other factors the committee took into account

Evidence identified from literature searches for review question 3 (risk factors for aneurysm growth or rupture in people with known AAA) established that women had a higher likelihood of aneurysm rupture than men. The committee agreed that including sex in the list of risk factors may remove focus from the risk of rupture in men. As a result, it was agreed that a separate recommendation should be made for women.

The committee discussed whether it was necessary to make a recommendation about imaging of suspected ruptures in non-specialist care settings.The committee noted that, when they reviewed evidence relating to imaging techniques for diagnosing unruptured and ruptured AAA , they recommended that an immediate bedside aortic ultrasound should be offered to people with suspected symptomatic or ruptured AAA. As a result, they did not think that repeating this recommendation was necessary. Instead, the committee opted to outline the importance of immediately discussing suspected ruptures with a vascular surgeon in order obtain specialist advice and facilitate prompt treatment.

Appendices

Appendix A – Review protocols

Review protocol for risk factors associated with aneurysm growth or rupture

Review question 15	Which signs, symptoms, risk factors (or combinations of these) and diagnostic assessment tools are most accurate in indicating the presence of a ruptured or symptomatic unruptured abdominal aortic aneurysm i) before arrival at the hospital and ii) in a non-specialist hospital setting?
Objectives	To determine which signs, symptoms and risk factors predict the presence of 'emergency' (that is, ruptured or symptomatic unruptured) abdominal aortic aneurysms To determine which signs, symptoms and risk factors would lead to immediate transfer to a regional vascular service (i.e. bypassing non-specialist A&E) To determine which signs, symptoms and risk factors should initiate definitive imaging in the emergency department (i.e. sufficient suspicion to initiate imaging, but not so high that a patient should be hurried on to vascular unit without imaging)
Type of review	Diagnostic
Language	English
Study design	Systematic reviews of study designs listed below Cross-sectional studies
Status	Published papers only (full text) No date restrictions
Population	People with a suspected ruptured or symptomatic unruptured abdominal aortic aneurysm
Index test / factors of interest	Pulsatile abdominal mass Abdominal, back or groin pain Sweating Clamminess Shock Altered mental/cognitive status Loss of consciousness Collapse Paralysis Dizziness Nausea Vomiting Hypotension Fast pulse / tachycardia Shortness of breath Cyanosis Urinary symptoms Colic Peripheral ischemia / absent peripheral pulses Temperature Capillary refill time Ultrasound ('fast scan')
Endpoint	Surgical or CT confirmation of rupture CT confirmation of AAA accompanied by symptoms

Review question 15	**Which signs, symptoms, risk factors (or combinations of these) and diagnostic assessment tools are most accurate in indicating the presence of a ruptured or symptomatic unruptured abdominal aortic aneurysm i) before arrival at the hospital and ii) in a non-specialist hospital setting?**
Other criteria for inclusion / exclusion of studies	Exclusion: Non-English language Abstract/non-published (i only)
Baseline characteristics to be extracted in evidence tables	Age Sex Size of aneurysm Comorbidities BMI
Search strategies	See Appendix B
Review strategies	Appropriate NICE Methodology Checklists, depending on study designs, will be used as a guide to appraise the quality of individual studies. 20% will be appraised by a second reviewer. Data on all included studies will be extracted into evidence tables. Where statistically possible, a meta-analytic approach will be used to give an overall summary effect. All key findings from evidence will be presented in GRADE profiles and further summarised in evidence statements.
Key papers	None identified

Appendix B – Literature search strategies

Clinical search literature search strategy

Main searches

Bibliographic databases searched for the guideline

- Cumulative Index to Nursing and Allied Health Literature - CINAHL (EBSCO)
- Cochrane Database of Systematic Reviews – CDSR (Wiley)
- Cochrane Central Register of Controlled Trials – CENTRAL (Wiley)
- Database of Abstracts of Reviews of Effects – DARE (Wiley)
- Health Technology Assessment Database – HTA (Wiley)
- EMBASE (Ovid)
- MEDLINE (Ovid)
- MEDLINE Epub Ahead of Print (Ovid)
- MEDLINE In-Process (Ovid)

Identification of evidence for review questions

The searches were conducted between November 2015 and October 2017 for 31 review questions (RQ). In collaboration with Cochrane, the evidence for several review questions was identified by an update of an existing Cochrane review. Review questions in this category are indicated below. Where review questions had a broader scope, supplement searches were undertaken by NICE.

Searches were re-run in December 2017.

Where appropriate, study design filters (either designed in-house or by McMaster) were used to limit the retrieval to, for example, randomised controlled trials. Details of the study design filters used can be found in section 4.

Search strategy review question 15

Medline Strategy, searched 29th September 2016 **Database: 1946 to September Week 3 2016** **Search Strategy:**
1 Aortic Aneurysm, Abdominal/
2 Aortic Rupture/
3 (aneurysm* adj4 (abdom* or thoracoabdom* or thoraco-abdom* or aort* or spontan* or juxtarenal* or juxta-renal* or juxta renal* or paraerenal* or para-renal* or para renal* or suprarenal* or supra renal* or supra-renal* or short neck* or short-neck* or shortneck* or visceral aortic segment*)).tw.
4 or/1-3
5 prognosis.sh.
6 diagnosed.tw.
7 cohort.mp.
8 predictor:.tw.
9 death.tw.

Medline Strategy, searched 29th September 2016 Database: 1946 to September Week 3 2016 Search Strategy:	
10	exp models, statistical/
11	or/5-10
12	(sensitiv: or predictive value:).mp. or accurac:.tw.
13	11 or 12
14	"signs and symptoms"/
15	((sign or signs) adj5 symptom*).tw.
16	Risk Factors/
17	factor*.tw.
18	predict*.tw.
19	or/14-18
20	13 or 19
21	4 and 20
22	animals/ not humans/
23	21 not 22 (12444)
24	limit 23 to english language

Health Economics literature search strategy

Sources searched to identify economic evaluations

- NHS Economic Evaluation Database – NHS EED (Wiley) last updated Dec 2014
- Health Technology Assessment Database – HTA (Wiley) last updated Oct 2016
- Embase (Ovid)
- MEDLINE (Ovid)
- MEDLINE In-Process (Ovid)

Search filters to retrieve economic evaluations and quality of life papers were appended to the population and intervention terms to identify relevant evidence. Searches were not undertaken for qualitative RQs. For social care topic questions additional terms were added. Searches were re-run in September 2017 where the filters were added to the population terms.

Health economics search strategy

Medline Strategy	
Economic evaluations	
1	Economics/
2	exp "Costs and Cost Analysis"/
3	Economics, Dental/
4	exp Economics, Hospital/
5	exp Economics, Medical/
6	Economics, Nursing/
7	Economics, Pharmaceutical/
8	Budgets/
9	exp Models, Economic/
10	Markov Chains/
11	Monte Carlo Method/

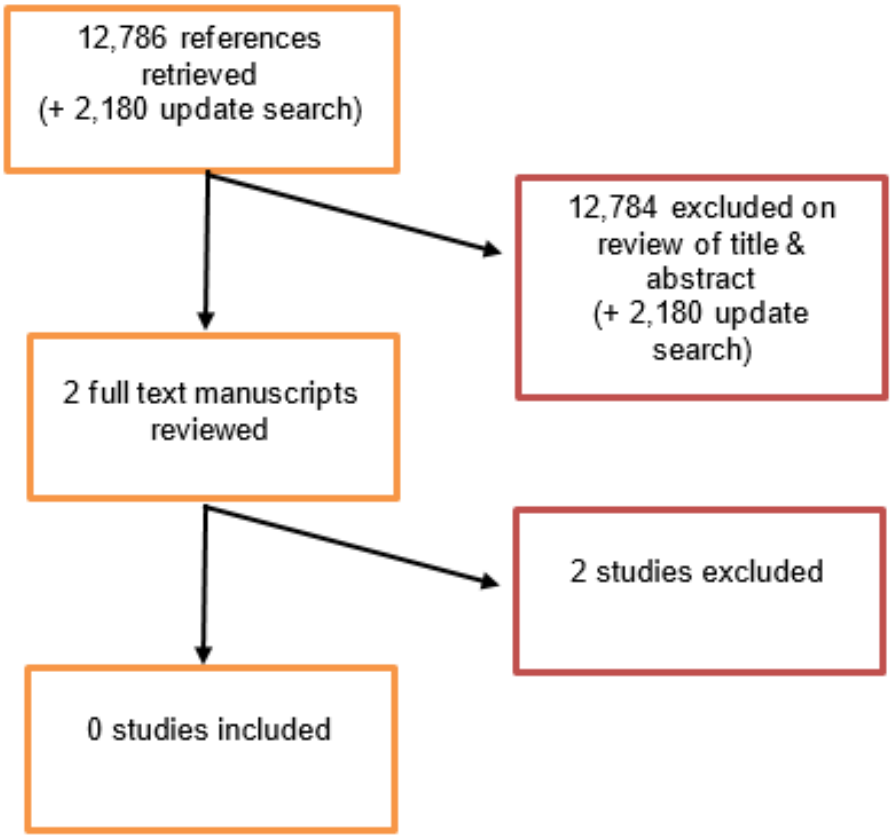
Medline Strategy

12 Decision Trees/
13 econom*.tw.
14 cba.tw.
15 cea.tw.
16 cua.tw.
17 markov*.tw.
18 (monte adj carlo).tw.
19 (decision adj3 (tree* or analys*)).tw.
20 (cost or costs or costing* or costly or costed).tw.
21 (price* or pricing*).tw.
22 budget*.tw.
23 expenditure*.tw.
24 (value adj3 (money or monetary)).tw.
25 (pharmacoeconomic* or (pharmaco adj economic*)).tw.
26 or/1-25

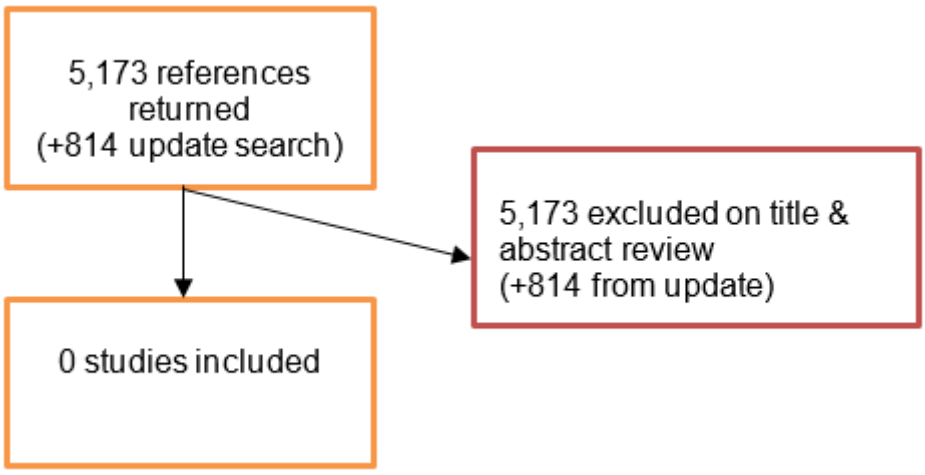
Quality of life
1 "Quality of Life"/
2 quality of life.tw.
3 "Value of Life"/
4 Quality-Adjusted Life Years/
5 quality adjusted life.tw.
6 (qaly* or qald* or qale* or qtime*).tw.
7 disability adjusted life.tw.
8 daly*.tw.
9 Health Status Indicators/
10 (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.
11 (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
12 (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw.
13 (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw.
14 (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw.
15 (euroqol or euro qol or eq5d or eq 5d).tw.
16 (qol or hql or hqol or hrqol).tw.
17 (hye or hyes).tw.
18 health* year* equivalent*.tw.
19 utilit*.tw.
20 (hui or hui1 or hui2 or hui3).tw.
21 disutili*.tw.
22 rosser.tw.
23 quality of wellbeing.tw.
24 quality of well-being.tw.
25 qwb.tw.
26 willingness to pay.tw.
27 standard gamble*.tw.

Medline Strategy	
28	time trade off.tw.
29	time tradeoff.tw.
30	tto.tw.
31	or/1-30

Appendix C – Clinical evidence study selection



Appendix D – Economic evidence study selection



Appendix E – Excluded studies

Clinical studies

No.	Study	Reason for exclusion
1	Iino Misako, Kuribayashi Sachio, Imakita Satoshi, Takamiya Makoto, Matsuo Hiroshi, Ookita Yutaka, Ando Motomi, and Ueda Hatsue (2002) Sensitivity and specificity of CT in the diagnosis of inflammatory abdominal aortic aneurysms. Journal of computer assisted tomography 26(6), 1006-12	The study explored the diagnostic accuracy of CT scans for detecting inflamed abdominal aortic aneurysms. It was not specified which setting (specialist versus non-specialist) the scans were performed.
2	Maybury Rubie Sue, Chang David C, and Freischlag Julie A (2011) Rural hospitals face a higher burden of ruptured abdominal aortic aneurysm and are more likely to transfer patients for emergent repair. Journal of the American College of Surgeons 212(6), 1061-7	Case control evaluating medical records of people with a diagnosis of intact AAA who underwent surgical repair or people with a diagnosis of ruptured AAA upon presentation to a healthcare facility.

Economic studies

No full text papers were retrieved. All studies were excluded at review of titles and abstracts.

Appendix F – Glossary

Abdominal Aortic Aneurysm (AAA)

A localised bulge in the abdominal aorta (the major blood vessel that supplies blood to the lower half of the body including the abdomen, pelvis and lower limbs) caused by weakening of the aortic wall. It is defined as an aortic diameter greater than 3 cm or a diameter more than 50% larger than the normal width of a healthy aorta. The clinical relevance of AAA is that the condition may lead to a life threatening rupture of the affected artery. Abdominal aortic aneurysms are generally characterised by their shape, size and cause:

- Infrarenal AAA: an aneurysm located in the lower segment of the abdominal aorta below the kidneys.
- Juxtarenal AAA: a type of infrarenal aneurysm that extends to, and sometimes, includes the lower margin of renal artery origins.
- Suprarenal AAA: an aneurysm involving the aorta below the diaphragm and above the renal arteries involving some or all of the visceral aortic segment and hence the origins of the renal, superior mesenteric, and celiac arteries, it may extend down to the aortic bifurcation.

Abdominal compartment syndrome

Abdominal compartment syndrome occurs when the pressure within the abdominal cavity increases above 20 mm Hg (intra-abdominal hypertension). In the context of a ruptured AAA this is due to the mass effect of a volume of blood within or behind the abdominal cavity. The increased abdominal pressure reduces blood flow to abdominal organs and impairs pulmonary, cardiovascular, renal, and gastro-intestinal function. This can cause multiple organ dysfunction and eventually lead to death.

Cardiopulmonary exercise testing

Cardiopulmonary Exercise Testing (CPET, sometimes also called CPX testing) is a non-invasive approach used to assess how the body performs before and during exercise. During CPET, the patient performs exercise on a stationary bicycle while breathing through a mouthpiece. Each breath is measured to assess the performance of the lungs and cardiovascular system. A heart tracing device (Electrocardiogram) will also record the hearts electrical activity before, during and after exercise.

Device migration

Migration can occur after device implantation when there is any movement or displacement of a stent-graft from its original position relative to the aorta or renal arteries. The risk of migration increases with time and can result in the loss of device fixation. Device migration may not need further treatment but should be monitored as it can lead to complications such as aneurysm rupture or endoleak.

Endoleak

An endoleak is the persistence of blood flow outside an endovascular stent - graft but within the aneurysm sac in which the graft is placed.

- Type I – Perigraft (at the proximal or distal seal zones): This form of endoleak is caused by blood flowing into the aneurysm because of an incomplete or ineffective seal at either end of an endograft. The blood flow creates pressure within the sac and significantly increases the risk of sac enlargement and rupture. As a result, Type I endoleaks typically require urgent attention.

- Type II – Retrograde or collateral (mesenteric, lumbar, renal accessory): These endoleaks are the most common type of endoleak. They occur when blood bleeds into the sac from small side branches of the aorta. They are generally considered benign because they are usually at low pressure and tend to resolve spontaneously over time without any need for intervention. Treatment of the endoleak is indicated if the aneurysm sac continues to expand.

- Type III – Midgraft (fabric tear, graft dislocation, graft disintegration): These endoleaks occur when blood flows into the aneurysm sac through defects in the endograft (such as graft fractures, misaligned graft joints and holes in the graft fabric). Similarly to Type I endoleak, a Type III endoleak results in systemic blood pressure within the aneurysm sac that increases the risk of rupture. Therefore, Type III endoleaks typically require urgent attention.

- Type IV– Graft porosity: These endoleaks often occur soon after AAA repair and are associated with the porosity of certain graft materials. They are caused by blood flowing through the graft fabric into the aneurysm sac. They do not usually require treatment and tend to resolve within a few days of graft placement.

- Type V – Endotension: A Type V endoleak is a phenomenon in which there is continued sac expansion without radiographic evidence of a leak site. It is a poorly understood abnormality. One theory that it is caused by pulsation of the graft wall, with transmission of the pulse wave through the aneurysm sac to the native aneurysm wall. Alternatively it may be due to intermittent leaks which are not apparent at imaging. It can be difficult to identify and treat any cause.

Endovascular aneurysm repair

Endovascular aneurysm repair (EVAR) is a technique that involves placing a stent –graft prosthesis within an aneurysm. The stent-graft is inserted through a small incision in the femoral artery in the groin, then delivered to the site of the aneurysm using catheters and guidewires and placed in position under X-ray guidance.

- Conventional EVAR refers to placement of an endovascular stent graft in an AAA where the anatomy of the aneurysm is such that the ‘instructions for use’ of that particular device are adhered to. Instructions for use define tolerances for AAA anatomy that the device manufacturer considers appropriate for that device. Common limitations on AAA anatomy are infrarenal neck length (usually >10mm), diameter (usually ≤30mm) and neck angle relative to the main body of the AAA

- Complex EVAR refers to a number of endovascular strategies that have been developed to address the challenges of aortic proximal neck fixation associated with complicated aneurysm anatomies like those seen in juxtarenal and suprarenal AAAs.

These strategies include using conventional infrarenal aortic stent grafts outside their 'instructions for use', using physician-modified endografts, utilisation of customised fenestrated endografts, and employing snorkel or chimney approaches with parallel covered stents.

Goal directed therapy

Goal directed therapy refers to a method of fluid administration that relies on minimally invasive cardiac output monitoring to tailor fluid administration to a maximal cardiac output or other reliable markers of cardiac function such as stroke volume variation or pulse pressure variation.

Post processing technique

For the purpose of this review, a post-processing technique refers to a software package that is used to augment imaging obtained from CT scans, (which are conventionally presented as axial images), to provide additional 2- or 3-dimensional imaging and data relating to an aneurysm's, size, position and anatomy.

Permissive hypotension

Permissive hypotension (also known as hypotensive resuscitation and restrictive volume resuscitation) is a method of fluid administration commonly used in people with haemorrhage after trauma. The basic principle of the technique is to maintain haemostasis (the stopping of blood flow) by keeping a person's blood pressure within a lower than normal range. In theory, a lower blood pressure means that blood loss will be slower, and more easily controlled by the pressure of internal self-tamponade and clot formation.

Remote ischemic preconditioning

Remote ischemic preconditioning is a procedure that aims to reduce damage (ischaemic injury) that may occur from a restriction in the blood supply to tissues during surgery. The technique aims to trigger the body's natural protective functions. It is sometimes performed before surgery and involves repeated, temporary cessation of blood flow to a limb to create ischemia (lack of oxygen and glucose) in the tissue. In theory, this "conditioning" activates physiological pathways that render the heart muscle resistant to subsequent prolonged periods of ischaemia.

Tranexamic acid

Tranexamic acid is an antifibrinolytic agent (medication that promotes blood clotting) that can be used to prevent, stop or reduce unwanted bleeding. It is often used to reduce the need for blood transfusion in adults having surgery, in trauma and in massive obstetric haemorrhage.