NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of artificial heart implantation as a bridge to transplantation for end-stage refractory biventricular heart failure

End-stage biventricular heart failure means that both sides of the heart are no longer strong enough to pump blood around the body for it to function adequately. An artificial heart implant involves removing the weakened 2 lower chambers and 4 valves of the heart and fixing a mechanical device to take over their role. The device is either powered by batteries or an external power supply. It can be used for people who are waiting for a heart transplant and are at risk of death. The aim is to extend life until a donor heart becomes available for transplantation.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this interventional procedure (IP) overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This IP overview was prepared in June 2017.

Procedure name

- Artificial heart implantation as a bridge to transplantation for end-stage refractory biventricular heart failure

Specialist societies

- Society of Cardiothoracic Surgeons of Great Britain and Ireland
- British Society for Heart Failure

- Royal College of Surgeons (England).

Description

Indications and current treatment

Biventricular heart failure results from structural or functional abnormalities of the heart. It leads to reduced blood flow to body tissues and oedema in the lungs (causing breathlessness) and the periphery (causing swelling of the legs). Other symptoms include reduced exercise tolerance, fatigue and malaise.

Medical treatment of heart failure involves drugs, such as diuretics and inotropic agents, to improve heart function. Invasive therapies such as electrophysiological interventions, coronary revascularisation, valve replacement or repair, may also be used for patients with end-stage refractory biventricular heart failure. When these therapies no longer work, left ventricular or biventricular assist devices or heart transplantation may be considered.

What the procedure involves

A total artificial heart (TAH) can be implanted to provide circulatory support with the aim that the patient survives while waiting for a donor heart to become available (a technique known as bridge-to-transplantation). In this procedure the device replaces the heart function completely.

Implantation of a TAH is done with the patient under general anaesthesia and on cardiopulmonary bypass. The native left and right ventricles, and all 4 cardiac valves are excised. The TAH device is implanted and attached to the atria, for blood inflow, and pulmonary artery and aorta, for blood outflow. Depending on the type of TAH, power is supplied either by drive lines connected percutaneously to an external biventricular pneumatic pump (which may be portable or static) or by batteries which are implanted internally and can be recharged through the skin using a transcutaneous energy transfer system. When the device begins to pump and restores blood flow around the body, cardiopulmonary bypass is stopped and the chest incision is closed.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to artificial heart implantation as a bridge to transplantation for end-stage refractory biventricular heart failure. The following databases were searched, covering the period from their start to 03.03.2017: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also

searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with end-stage refractory biventricular heart failure.
Intervention/test	Artificial heart implantation as a bridge to transplantation.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 1166 patients from 3 non-randomised retrospective studies[1,3,4], 5 case series[2, 5,6,7, 8] and 3 case reports[9,10,11]. Of these, 698 patients had total heart implantations as a bridge to transplantation.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on artificial heart implantation as a bridge to transplantation for end-stage refractory biventricular heart failure

Study 1 Copeland JG (2004)

Details

Study type	Non-randomised prospective comparative study
Country	US (multicentre)
Recruitment period	1993-2003
Study population and number	n=130 (**81 patients with biventricular cardiac failure bridged to transplantation with total artificial heart (TAH), 35 matched historical controls and 14 patients who did not meet the protocol-inclusion criteria but in whom the TAH was implanted on a compassionate basis)** Body surface area: mean 2.0 m^2
Age and sex	Study group: mean 51 years; control group: mean 52 years Study group: 86% male; control group: 91% male
Patient selection criteria	Inclusion criteria: transplant eligible patients at risk of imminent death from irreversible biventricular cardiac failure, NHYA class IV, body surface area 1.7 to 2.5 m^2 or a distance of >10 cm from the anterior vertebral body to inner table of the sternum at 10^{th} thoracic vertebra on CT scanning, haemodynamic insufficiency (cardiac index >2.0 litres/min/m^2 and systolic arterial pressure <90 mmHg or central venous pressure >18 mmHg, dopamine at a dose of >10 µg/kg body weight/min, dobutamine at a dose of>10 µg/kg/min epinephrine at a dose of >2 µg/kg/min, other cardio active drugs at maximal doses, use of an intra-aortic balloon pump, or use of cardiopulmonary bypass. Exclusion criteria: use of any vascular assist device, pulmonary vascular resistance>640 dyn.sec.cm-5, dialysis in previous 7 days, serum creatinine > 5mg/dl (440 µmol/litre), cirrhosis with total bilirubin >5 mg/dl (29 µmol/litre), cytotoxic antibody>10%.
Technique	Total artificial heart (TAH) implantation (CardioWest TAH, Syncardia Systems) as a bridge to transplantation in study group. Coagulation monitoring and anticoagulation were performed. In 13 patients the device was implanted on a compassionate basis. Control patients were matched with the study group according to selection criteria but did not receive any mechanical circulatory support.
Follow-up	**5 years post transplantation**
Conflict of interest/source of funding	Not reported

Analysis

Study design issues: prospective study in 5 centres, control group patients were found on retrospective review of records. Primary endpoints include rates of survival to heart transplantation and of survival after transplantation. Other outcomes included overall survival, treatment success (defined as alive after 30 days, NYHA class I or II, no dependant on ventilator and not undergoing dialysis), haemodynamic recovery, recovery of end organ function, percentage of patients who were ambulatory and who could walk more than 100 feet. Data from the control groups was only used for survival comparisons.

Study population issues: patients were mainly with heart failure in whom inotropic therapy failed and were not suitable for the use of a left ventricular assist device. Baseline characteristics of the 2 groups differed significantly and the control group is not an exact match but provides an estimation of the natural history of patients with cardiogenic shock.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **81 study versus 35 control**

Survival outcomes

	TAH group (n=81)	Control group (n=35)	p value
Survival to transplantation %	79 (95% CI 68 to 87)	46	<0.001
Mean time to transplantation or death (days)	79.1	8.5	<0.001
Overall survival at 1 year %	70 (95% CI 63 to 77)	31	<0.001
Survival at 1 year after transplantation %	86	69	
Survival at 5 years after transplantation %	64	34	
Treatment success %	69	37	0.002

Rate of survival to transplantation in patients who were treated off protocol (n=14) was 50%.

Haemodynamic and other outcomes

Haemodynamic status improved after implantation with a sustained increase in the cardiac index from baseline 1.9 to 3.2 litres/min/square metre body surface area, mean systolic arterial pressure rose from 93 to 122 mm Hg, mean central venous pressure fell from 20 to 14 mm Hg, the organ perfusion pressure rose from 49 to 68 mm Hg. Renal and hepatic function and the levels of blood urea nitrogen, creatinine, bilirubin, and liver enzymes returned to normal within 3 weeks. Other laboratory values such as electrolyte levels, platelet count, and the white blood cell count also returned to normal at 3 to 4 weeks.

Quality of life

Quality of life in study group patients improved significantly: 75% of patients were out of bed 1 week after implantation. Mobility (defined as ability to walk more than 100 feet) was observed in 60.5% patients.

Safety

Adverse events (from study entry to 30 days after transplantation)

Adverse event	% (n=95)*	No of events	Deaths
Bleeding (50% occurred during implantation-mainly tamponade or mediastinal bleeding needed surgery and blood transfusion within 21 days)	62 (59/95)	102	2 (1 at implantation 1 at transplantation)
Device malfunction	17 (16/95)	19	1 (perforation in one of the layers of device's left ventricular diaphragm on day 124)
Fitting complication (3 repositioned in repeat surgery)	5 (5/95)	5	2 (due to poor fit)
Reduced cardiac index associated with 8 events (<2 litres/min/square metre for 4 hours or more during first 11 days)	9 (9/95)	13	0
Reduced blood pressure	19 (18/95)	27	2
Haemolysis	4 (4/95)	5	0
Hepatic dysfunction	37 (35/95)	37	0
Infection (in blood, respiratory, mediastinal, urinary, GI, driveline and catheters; delayed transplant in 5)	77 (73/95)	172	1 (infection contributed to 7 other deaths)
Neurologic events (stroke in 10, TIA 4, anoxic encephalopathy in 5, metabolic encephalopathy in 1, seizure in 4, syncope in 1; 6 delayed transplantation)	27 (26/95)	35	0
Operation	24 (23/95)	31	0
Peripheral thromboembolism	14 (13/95)	18	0

Renal dysfunction	31 (29/95)	34	0
Respiratory dysfunction	36 (34/95)	61	0
Technical or procedural problem (mechanical tricuspid valve of TAH obstructed as a result of migration of central venous catheter)	3 (3/95)	11	1
Other problems	9 (9/95)	10	1

*includes both study patients (n=81) and patients who had TAH implantation on a compassionate basis (n=13).

Mortality

	Study group % (n=81)	**Control group % (n=35)**
Death before transplantation	21 (17/81)	54 (19/35)
Causes		
Cardiac arrest		7
Congestive heart failure	1	7
Multi-organ failure	7	3
Graft failure/acute rejection		1
Pulmonary oedema	1	1
Procedural or technical complications	4	0
Bleeding	2	0
Sepsis	2	0
Death after transplantation	6 (3 graft failure, 1 sepsis, 1 procedural or technical complications and 1 multi-organ failure)	2 (1 acute rejection and 1 multi-organ failure)

Abbreviations used: CI, confidence interval; GI, gastrointestinal; TAH, total artificial heart; TIA, transient ischaemic attack.

Study 2 Copeland JG (2012)

Details

Study type	Case series
Country	US (single centre)
Recruitment period	1993-2009
Study population and number	n=**101 patients bridged to transplantation with total artificial heart** Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profile 1 or 1A: 91% patients, (INTERMACS profile 2): 9% Mean body surface area (BSA): 2.05 m^2, mean weight 85 kg, NYHA class 1: 93%
Age and sex	Mean age 48 years; 85% (86/101) male
Patient selection criteria	Inclusion criteria: transplant eligible patients, NHYA class IV, body surface area 1.7 to 2.5 m^2 or a distance of >10 cm from the anterior vertebral body to inner table of the sternum at 10th thoracic vertebra on CT scanning, haemodynamic insufficiency (cardiac index >2.0 litres/min/m^2 and systolic arterial pressure <90 mmHg or central venous pressure >18 mmHg, or on 2 of the following: dopamine at a dose of >10 µg/kg body weight/min, dobutamine at a dose of >10 µg/kg/min epinephrine at a dose of >2 µg/kg/min, other cardio active drugs at maximal doses, use of an intra-aortic balloon pump, or use of cardiopulmonary bypass. Compassionate use cases were included. Exclusion criteria: use of any vascular assist device, pulmonary vascular resistance >640 dyn.sec.cm-5, dialysis in previous 7 days, serum creatinine >5 mg/dl (440 µmol/litre), cirrhosis with total bilirubin > 5mg/dl (29 µmol/litre), cytotoxic antibody >10%.
Technique	Total artificial heart (TAH) implantation (Syncardia TAH, Syncardia Systems) as a bridge to transplantation. Coagulation monitoring and anticoagulation strategies were performed in all. A polytetrafluorethylene neopericardium was constructed to cover the TAH in 70 patients. All were on in-hospital device support.
Follow-up	**10 years**
Conflict of interest/source of funding	The primary author reports equity ownership and service as a board member of Syncardia Systems.

Analysis

Study design issues: retrospective study, chart review of database; adverse events were defined according to FDA investigational device exemption trial.

Study population issues: study selection criteria were liberalised and patients who were too sick to meet the eligibility for cardiac transplantation were accepted for implantation. 9 patients had a BSA of 1.77m^2. 41 patients had mechanical ventilation, 26 were on mechanical circulatory support, 26 had a recent cardiac arrest and 4 were on extracorporeal membrane oxygenation.

Other issues: 65 of these patients are reported as part of the multicentre study 1 from 1993-2002 (Copeland 2004). So there is an overlap of patients with study 1.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **101**

Outcomes	
Mean support time (days)	87±94.8 (median 53, range 1 to 144)
Pump outputs during support (L/min)	7 to 9
Survival to transplantation % (n)	68.3 (69/101)
Survival after transplantation % (n)	
1 year % (n=69)	76.8
5 year %	60.5
10 year (n=18)	41.2
Overall survival (all patients who received implants) % (n)	
1 year	55.4 (n=56)
5 years	42.6 (n=35)
10 years	28.1 (n=18)
15 years	26.1 (n=3)

The longest survivor is alive 16.4 years post implantation.

Safety

Adverse event	**% (n)**	**Timing**
Neurologic	**16 (16/101)**	
Stroke	8 (8/101)	5 events by 9 days and 3 thereafter.
Peripheral emboli (at celiac artery 1, spleen 2, superior mesenteric artery 1, kidney 2, retina 2)	8 (8/101)	3 at <7 days, 5 at 38 to 286 days 4 died.
Bleeding (from various sites)	**43 (43/101)**	
Reoperations for haemorrhage (mediastinal explorations)	25 (25/101)	11 in 24 hours, mean 4.2 days
Infection (common sites lung and urinary tract, all treated- 3 had clinical mediastinitis)	**64 (64/101)**	50% in first 30 days
Catheter entrapment of a central line in the tricuspid valve (leading to brain damage from cardiac arrest, both died)	**2**	
Deaths on device support (70% were within 14 days)	**32 (32/101)**	
Multiple organ failure	13	
Pulmonary failure (oedema or pneumonia)	6	
Sepsis	5	
Neurologic injury (1 stroke, 1 hypoxic damage from hypotension, 2 intracranial haemorrhage)	4	
Pancreatic abscess	1	
Small intestinal ischaemia	1	
Disseminated intravascular coagulopathy	1	
Disseminated coccidiodomycosis	1	

At explantation it was found that PTFE neopericardium decreased adhesion formation and the 'skin to recannulation time was 15 to 45 minutes.

Abbreviations used: INTERMACS, interagency registry for mechanically assisted circulatory support; PTFE, polytetrafluoroethylene.

Study 3 Cheng A (2016)

Details

Study type	Non-randomised retrospective comparative study (United Network of Organ Sharing (UNOS) database analysis)
Country	US
Recruitment period	2005-2014
Study population and number	n=**212 Total artificial heart (TAH) versus 366 biventricular ventricular assist device (BIVAD) as a bridge to heart transplantation (BTT) in adult patients.**
Age and sex	TAH Mean 49.8 years; BIVAD mean 47.2 years (p=0.04). TAH 87% versus 74% male (p<0.0001). BMI: TAH 27.3 versus BIVAD 25.6 (p<0.0001); mean pulmonary arterial pressure (33.4 versus 30.5 mm Hg, p=0.02); creatinine (1.7 versus 1.3 mg/dl, p<0.009). UNOS status 1A : 94% versus 86 (p=0.002)
Patient selection criteria	Patients aged >18 years old who underwent heart transplantation between 2005 and 2014 were included. Patients with no mechanical ventilator support at the time of transplant, those with mechanical circulatory support other than Syncardia TAH , biventricular Thoratec paracorporeal pVAD, Thoratec implantable iVAD, Heartmate II, or Heartware HVAR at the time of transplantation, patients with short term right ventricular support (for example Centrimag) were excluded from the analysis.
Technique	Total artificial heart (TAH) implantation (Syncardia TAH, Syncardia Systems) or BIVAD as a bridge to transplantation. BIVAD: included 344 patients with pulsatile-flow devices and 22 with continuous flow devices.
Follow-up	**3 years**
Conflict of interest/source of funding	The study was sponsored by funds from the Health Resources and Services Administration contract.

Analysis

Study design issues: retrospective comparative analysis between 2 interventions using data from a national UNOS database. Kaplan–Meier survival curves were examined to assess the differences in wait-list (post-implantation) and post-transplant survival between groups. Cox regression model was used to study the hazard ratios of the association between TAH versus BIVAD support and post-transplant survival. Propensity matching was not performed. Patients with TAH or BIVAD support not listed for transplant were not included in the analysis. Not all complications before heart transplantation were reported in the database and therefore were not compared within groups.

Study population issues: out of a total 17,022 patients who underwent heart transplantation only 212 patients underwent TAH implantation. Patient characteristics before device implantation and duration of support were not available from the database. The number of continuous flow BIVAD devices placed were low.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **TAH 212 versus BIVAD 366**

Survival estimates (Kaplan–Meier curves)

	TAH %	BIVAD %	p value
Post- implantation			
30 days	95	93	
1 year	77	69	0.8
Post-transplant			
30 day survival rate	88	93	
1 year survival rate	78	83	
3 year survival rate	67	73	0.06

Cox regression model for post-transplant survival

Cox regression model shows that TAH is not associated with a worse post-transplant survival when compared to BIVAD (p=0.1).

Increased pre-transplant creatinine (HR=1.21, p=0.008) was associated with a lower post-transplant survival.

There was no significant difference in wait-list survival (p=0.58) or post-transplant survival (p=0.19) between the 2 types of support.

Safety

Complication rate post-implantation

Complications post-implantation %	TAH % (n)	BIVAD % (n)	p value
Renal failure/dialysis	24 (54/212)	10 (35/366)	<0.0001
Infection	22 (46/212)	28 (104/366)	0.005

Complication rates after transplantation

Complications after transplantation %	TAH % (n)	BIVAD % (n)	p value
Stroke	6.6 (14/212)	4.5 (16/366)	0.3
Renal failure/dialysis	26 (56/212)	14 (49/366)	0.0001
Need for pacemaker	4.3 (9/212)	3.0 (11/366)	0.07
Graft failure	11 (23/212)	9 (32/366)	0.4

Deaths post implantation

Cause of death post device implantation %	TAH % (n)	BIVAD % (n)	p value
Number of deaths , n	22	45	0.7
Infection: septicaemia	5 (1/22)	9 (4/45)	0.2
Multiple organ failure	36 (8/22)	31 (14/45)	0.3
Stroke or haemorrhage	23 (5/22)	18 (8/45)	0.7

Deaths post-transplantation

Cause of death after transplantation %	TAH % (n)	BIVAD % (n)	p value
Number of deaths, n	64	111	0.9
Acute rejection	11 (7/64)	4.5 (5/111)	0.4
Infection: septicaemia	14 (9/64)	7 (6/111)	0.2
Cardiac arrest	4 (3/64)	10 (11/111)	0.5
Multiple organ failure	17 (11/64)	5 (6/111)	0.2
Stroke	1.5 (1/64)	1.8 (2/111)	0.9

Abbreviations used: BIVAD, biventricular assist device; HR, hazard ratio; TAH, total artificial heart.

Study 4 Nguyen A (2014)

Details

Study type	Non-randomised retrospective comparative study
Country	France
Recruitment period	1996-2009
Study population and number	n=**148 patients undergoing planned biventricular support (81 Total artificial heart (TAH) implantation versus 67 paracorporeal biventricular ventricular assist device (p-BIVAD) as a bridge to heart transplantation (BTT).**
Age and sex	Mean age 43.7 years. 86% male (128/148).
Patient selection criteria	Patients who suffered primary biventricular failure, who had planned biventricular support as a bridge to transplantation or recovery and those receiving biventricular support using Thoratec p-BIVADs and Syncardia devices were included. Patients receiving biventricular support for post-cardiotomy shock, early cardiac allograft failure or after failed isolated LVAD implantation and patients receiving right ventricular assist device using a temporary device were excluded.
Technique	Total artificial heart (TAH) (Syncardia CardioWest TAH, Syncardia Systems) implanted. Mobile and portable drivers have been used in few patients. Paracorporeal BIVAD: Thoratec a pulsatile paracorporeal ventricular assist device was implanted. Left heart support was achieved by cannulating the apex of the left ventricle and the ascending aorta. Right heart support was achieved by cannulating the right atrium or the right ventricle and the pulmonary artery. A portable driver allows improved patient mobility. Antithrombotic regimen used in both groups, in the TAH group it evolved over study period.
Follow-up	**5 years**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Long term follow-up of transplanted patients averaged 53±43.9 months; cumulative follow-up was 4783 patient-months.

Study design issues: small retrospective comparative study in 2 teaching hospitals and spanned over a long time period. Medical records were reviewed retrospectively to collect data. Survival data were analysed with Kaplan–Meier techniques, Cox regression analysis was done to identify predictors for death while on mechanical circulatory support.

Study population issues: BIVAD patient cohort were from 1 centre and TAH patient cohort were from another centre. There were significant pre-implant differences between patient groups as some data were missing in more than 50% patients. Patients receiving TAH had more frequently a history or prior cardiac surgery and had higher rates of pre-implant extracorporeal life support and hemofiltration. Patients receiving BIVAD had significantly lower pre-implant blood pressures and more severe hepatic cytolysis, higher white blood cells, a tendency towards higher rates of acute myocardial infarction and need for resuscitation before implantation.

Other issues: authors conclude that the success of bridge to transplantation is mainly driven by the patients' pre-implant condition rather than the device used for support.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **TAH 81 versus p-BIVAD 67**

Survival outcomes

	TAH	p-BIVAD	p value
Duration of support (days)	71.4±92.1	79.3±100.2	0.62
Survival on device support	n=81	n=67	0.87
30 days	76.0±5.4	72.1±5.2	
60 days	61.7±6.6	63.6±6.1	
180 days	53.4±8.1	46.1±8.7	
Post-transplant survival	n=51	n=39	0.60
30 days	82.4±5.3	81.4±6.3	
1 year	77±6	76±7	
3 years	72±6	70±8	
5 years	70±7	58±9	

12 patients with TAH were discharged home using portable drivers and 3 patients with BIVAD were weaned off support at a mean of 44 days, however 1 underwent transplantation after 94 days.

Risk factors for death while on support

Multivariate analysis showed that only preimplant diastolic blood pressure and alanine amino transferase levels were significant predictors of death.

Safety

Adverse events post implantation

Cause of death post device implantation %	TAH % (n)	BIVAD % (n)	p value
Number of deaths on support , n	37 (30/81)	39 (26/67)	0.87
Stroke	12 (9/81)	24 (16/67)	0.08
Reoperation for cannulae/driveline infection	1 (1/81)	3 (2/67)	0.61
Reoperation for mediastinitis	12 (9/81)	5 (3/67)	0.14
Reoperation for bleeding/ hematoma	23 (17/81)	42 (28/67)	0.03

Abbreviations used: BIVAD, biventricular assist device; TAH, total artificial heart.

Study 5 Kirsch ME (2013)

Details

Study type	Case series (retrospective study)
Country	France (single centre)
Recruitment period	2000-2010
Study population and number	n=**90 patients receiving biventricular support with total artificial heart (TAH)** mean body surface areas 1.9±0.22m2
Age and sex	Mean age 46±13 years; 89% male (80/90)
Patient selection criteria	All causes of cardiac failure (cardiogenic shock secondary to idiopathic n=40, or ischaemic n=24, cardiomyopathy or other causes), patients deemed not to be adequate left ventricular assist device (LVAD) recipients because of significant right ventricular dysfunction on hemodynamic and echocardiographic parameters or associated end-organ dysfunction, patients with adequate body surface area from 1.7 to 2.5 m^2 or T10 distance from sternum to anterior vertebral body 10cm or greater were included.
Technique	Total artificial heart (TAH) (Syncardia CardioWest TAH, Syncardia Systems) implanted as a bridge to transplantation (BTT). In some patients mobile and portable drivers allowed out of hospital care. The standard procedure was modified by wrapping the device with a polytetrafluoroethylene membrane. The post-operative antithrombotic regimen evolved over time. Since 2008, the protocol was simplified by using intravenous non-fractioned heparin followed by low molecular weight heparin and fluindione before patient discharge. Platelet activity was controlled with aspirin and clopidrogel. Mean cardiopulmonary bypass and aortic cross-clamp times were 125.7 and 116.9 minutes respectively. One patient had chronic aortic dissection and needed concomitant prosthetic replacement of the ascending aorta.
Follow-up	**5 years**
Conflict of interest/source of funding	Not reported

Analysis

Study design issues: small retrospective study. Survival data was analysed using Kaplan–Meier techniques for estimation of survival probabilities. Univariate analysis was done to identify risk factors for death under support by comparing patients who died during support with those who survived to transplantation.

Study population issues: 21% (17/90) patients had a history of previous cardiac surgery including coronary bypass grafting (n=7), heart valve surgery (n=6), orthotropic heart transplantation (n=3), and congenital heart surgery (n=1). 33% (27/90) patients needed mechanical ventilation at a mean of 5.9 days before implantation. 28% (23/90) patients needed mechanical circulatory support using either intra-aortic balloon pump (n=5), extracorporeal life support (n=12) or both (n=6) at a mean 8.0 days before implantation. 10% (8/90) received hemofiltration at a mean 6.3 days before implantation.

Pre-implant creatinine values were 1.7mg/dL and total bilirubin levels were 45µmol/l.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **90 TAH**

Outcomes under support

	TAH
Total duration of support (patient days)	7,532.0
Mean duration of support (days/per patient)	83.7±102.4
Actuarial survival under support (patients censored at the time of transplantation) (% survival)	
1 month	73.8±4.8
3 months	63.0±5.8
6 months	47.5±7.5

Patients were weaned from mechanical ventilation after a mean of 14.7 days and were discharged from intensive care

14% (12/90) patients were discharged home on mobile or portable devices while awaiting transplantation.

Overall survival after TAH implantation (patients not censored at time of transplantation)

Total follow-up after device implantation (patient months)	3,208.8
Mean follow-up (months per patient)	35.70±44.3
Overall survival estimates (% survival)	
1 month (% survival)	73.3±4.7
1 year	50.0±5.3
3 years	45.5±5.3
5 years	43.8±5.3

Outcomes after transplantation

Patients bridged to transplantation (after a mean of 97±98 days of support)	**61 (55/90)**
Total follow-up of transplanted patients (patient-months)	2,960.9
Mean follow-up (months per patient)	53.8±45.8
Actuarial survival after transplantation (% survival)	
1 month	83.6±5.0
1 year	78.2±5.6
3 years	74.0±6.0
5 years	71.2±6.4
8 years	63.1±7.8

Risk factors for death under support

Multivariate analysis identified older patient age and preoperative mechanical ventilation were risk factors for death while on support.

Safety

Adverse events on device support

	% (n)
Stroke	10 (9/90)
Bacterial mediastinitis (needing surgical debridement and closed drainage using catheters)	14 (13/90)
Surgical exploration for bleeding, hematoma or infection	39 (35/90)

Death on device support

	% (n)
Number of deaths on support (after a mean of 61.5±107.1 days)	39 (35/90)
Causes	
Multiple-organ dysfunction syndrome	19 (17/90)
Stroke	9 (8/90)
Cerebral bleeding (haemorrhagic stroke)	7 (6/90)
Ischaemic stroke	2 (2/90)
Bleeding	4 (3/90)
Infection	4 (3/90)
Gastrointestinal complication	1 (1/90)
Device failure	1 (1/90)
Unknown	4 (3/90)

Abbreviation used: TAH, total artificial heart.

Study 6 Torregrossa G (2014)

Details

Study type	Case series (retrospective study)
Country	Worldwide (10 centres: 3 from USA; 7 from Europe)
Recruitment period	1989-2011
Study population and number	n=**47 patients with biventricular failure supported with total artificial heart (TAH) for more than 1 year (long term support)** (Primary diagnosis: dilated cardiomyopathy (n=23), ischaemic (n=18), and other causes for heart failure (n=9). INTERMACS: class 1 (n=23); class II (n=7) and class III (n=3). Median body surface area(BSA): 2.02 m^2 (11 patients BSA value <1.8 m^2)
Age and sex	Mean age 50±1.57 years; 87% male (41/47).
Patient selection criteria	The study excluded patients supported for less than 1 year by TAH
Technique	Total artificial heart (TAH; Syncardia CardioWest TAH, Syncardia Systems) implanted as a bridge to transplantation (BTT).
Follow-up	**5 years**
Conflict of interest/source of funding	2 authors declared financial interest; One author is a co-founder of Syncardia and part of the board of directors, 1 author has been a consultant and proctor for Syncardia.

Analysis

Study design issues: review of medical records and hospital data; clinical data were collected on survival, infections, thromboembolic and haemorrhagic events, device failures and antithrombotic therapy. Individual institutions entered data into an online database and verified it.

Differences in surgical implantation technique adopted in the centres were not recorded. Patients were included over a broad time period and received TAH with improved technology and expertise.

Study population issues: it is not clear from the paper why these patients were supported for more than 1 year.

Other issues: the authors state that 'it is likely that complications experienced while under the use of TAH caused prolonged support times'.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **47 TAH**

Median support time (days)	554 (1.5 years) (range 365 to 1,374)
Cumulative support time (years)	79.8
Cardiac transplantation	72 (34/47)
Supported with device	(1/47)

85% (40/47) were discharged home, 1 was discharged with a portable unit.

Kaplan–Meier estimate of the overall survival according to BSA (<1.8 m^2 and >1.8 m^2) was significant p=0.0002. There were no differences in freedom from device failure, freedom from transplant survival and freedom from thromboembolic events.

Safety

Major complications

	% (n)
Adverse events after implantation	
Delayed sternal closure (median time 4 days)	23 (11/47)
Wound infection	4 (2/47)
Renal failure (needing postoperative RRT; recovery of renal function occurred in 73% [22/47] but RRT continued in 17% [8/47])	64 (30/47)
Complications under device support	
Deaths while on device support (within a median time of 525 days[range 381 to 971 days])	25 (12/47)
Device failure (membrane ruptured in 2 and the patients died, and 3 had nonfatal events: air hole in the driveline in 1, membrane rupture in 1 and lower pump output in1)	10 (5/47)
Systemic infections (needing antibiotics)	53 (25/47)
Driveline infections (superficial in 11, mediastinitis in 2 and 1 of them died; 5 died of sepsis with multi-organ failure)	27 (13/47)
Thromboembolic events (at a median time of 500 days; 6 had TIA, 3 suffered a major cerebrovascular accident with hemiparesis or aphasia)	19 (9/47)
Haemorrhagic events (at a median time of 249 days; cerebral haemorrhage in 3, subarachnoid haemorrhage in 2, gastrointestinal bleeding in 2)	14 (7/47)
Complications after transplantation	
Deaths after transplantation (at a median time of 145 days [range 50 to 328 days]) due to graft rejection	9 (3/34)

Patients with a BSA<1.8 m2, were found to have an increased incidence of death (p=0.0045), haemorrhagic events (p=0.009) and systemic infections (p=0.008).

Abbreviations used: BSA, body surface area; RRT, renal replacement therapy; TAH, total artificial heart; TIA, transient ischaemic attack.

Study 7 Demondion P (2013)

Details

Study type	Case series (retrospective study)
Country	France (single centre)
Recruitment period	2006-2010
Study population and number	n=**27 patients with biventricular heart failure implanted with total artificial heart (TAH)** Primary diagnosis: dilated cardiomyopathy (idiopathic n=14, ischaemic n=11), 1 toxic biventricular cardiomyopathy, 1 chronic rejection 8 years after an orthotropic heart transplant, 1 myocardial infarction with left ventricular wall rupture.
Age and sex	Median age 53 years; 96% male (26/27)
Patient selection criteria	Inclusion criteria for TAH were: evidence of haemodynamic decompensation, including cardiac index <2.0 1/min/m^2, central venous pressure >18 mmHg, high dose of inotropic agents, extracorporeal membrane oxygenation support or severe or repetitive ventricular arrhythmia. Patients with biventricular failure, intra-cardiac shunts or left ventricular thrombi which render them ineligible for LVAD implantation, selected cases involving primary graft failure or rejection were included.
Technique	Total artificial heart (TAH; Syncardia CardioWest TAH, Syncardia Systems) implanted as a bridge to transplantation (BTT). Since 2006, the device was connected to a smaller portable driver/console (Excor or Freedom). Follow-up consisted of a monthly hospital consultation aimed at checking device parameters, anticoagulation treatment, and other medical events. External console (Freedom) changed ever every month or every 10 million cycles (Excor). Anticoagulation protocol consisted of warfarin, clopidrogel and acetylsalicylic acid. Patients discharged home or to a rehabilitation centre were trained in autonomous device management, dealing with emergencies and well supervised by medical team. Once home they are followed up by a nurse for dressing and clinicians monthly or when needed. In addition they were well educated about anticoagulation treatment.
Follow-up	**Median 20 months**
Conflict of interest/source of funding	None declared

Analysis

Study design issues: small observational study which mainly reports outpatient management. Clinical and biological data (morbidity, mortality, causes of rehospitalisation, quality of life during home discharge, bridge to transplant results) have been retrospectively analysed. Definitions from Interagency Registry for Mechanically assisted Circulatory Support (INTERMACS) were used to categorise adverse events during in-hospital stay and in outpatients. The quality of life was assessed using a modified EQ-5D questionnaire defined by INTERMACS.

Study population issues: before implantation, 52% (14/27) patients were receiving mechanical support with extracorporeal life support, 3 had intra-aortic balloon pumps, 18 needed mechanical ventilation and 4 had cardiopulmonary resuscitation within 24 hours.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **27 TAH**

Support time, discharge and transplant results

Discharged home/rehabilitation centre from hospital (within a median of 88 days [range 35 to 152])*	44.4 (12/27)
Post-transplant survival (median follow-up 20 months) %	91

*Between discharge and transplant, patients spent 87% of their support time out of hospital. All patients who returned home with TAH were subsequently transplanted at a median time of 254 days after device implantation.

Quality of life for patients discharged

One young patient was able to return to school but none went back to work. All patients and families declared the consoles noise to be bothersome.

Safety

Major complications during hospitalisation

	% (n)
Deaths during device support (all before discharge, median time 26 days)	55.5 (15/27)
Causes of death	
Multi-organ failure (sepsis related in 2)	46.6 (12/27)
Bleeding complications	1
Mesenteric ischaemia	1
Cerebrovascular event	1
Adverse events	
Bacterial pneumonias	44 (12/27)
Bleeding events (mediastinal bleeding or atrial tamponade needing surgery first month after implantation)	40.7 (11/27)
Infections	
Driveline infections	6
Superficial sternal infections	2
Mediastinitis (treated by antibiotics and redo surgery, 2 were lethal)	6
Other events	
Acute respiratory distress syndrome (requiring ECMO, tracheostomy needed in 4)	6
Device malfunction (of control system, console changed)	1
Haemorrhagic complication of antivitamin K	1
Wound dehiscence	1
Arterial thromboembolism	1
Neurological dysfunction (ischaemic or haemorrhagic)	4

Adverse events after discharge

	% (n)
Deaths at home	**0**
Major infections	**7**
Driveline infections	3
Mediastinitis (median time 90 days, 2 operated)	4
Device malfunction	
Air leak on driveline (sealed)	2
Alarm triggering caused by auricular compression during movements	1
Neurological dysfunction (ischaemic cerebral accident)	1
Other (1 haemolysis)	3
Readmissions	14

Deaths after transplantation =1

Abbreviations used: TAH, total artificial heart; ECMO, extracorporeal membrane oxygenation.

Study 8 Morales DL (2016)

Details

Study type	Case series (retrospective study)
Country	Worldwide (mainly US)
Recruitment period	2005-2015
Study population and number	n=**43 adolescents with heart failure implanted with total artificial heart (TAH) as a bridge to transplantation** Primary diagnosis: dilated cardiomyopathy (42%), transplant rejection (19%), and congenital heart disease (16%).
Age and sex	Median 19 years age (range 9 to 21 years); 65% male
Patient selection criteria	All children less than 21 years old supported with TAH between 2005 and 2015 identified via the Syncardia TAH database.
Technique	Total artificial heart (TAH) (Syncardia TAH, Syncardia Systems) implanted as a bridge to transplantation (BTT) and supported with portable Freedom driver. Majority had 70 cc device.
Follow-up	**12 months**
Conflict of interest/source of funding	Primary author was an instructor, consultant for Syncardia and the primary investigator of the national 50/50 cc TAH FDA trial.

Analysis

Study design issues: limited data from the Syncardia database was analysed retrospectively. Data from 30 centres from 8 countries were included. Lack of patient specific data within the database.

Patient issues: 2 patients were converted to TAH after previous LVAD placement.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **43 TAH**

Clinical outcomes

Total support time	5757 days
Median patient support time (days)*	66
Positive outcome (transplant or alive on device) % (n)	
60 days	70 (30/43)
90 days	63 (27/43)
120 days	58 (25/43)
Patients supported with portable device (n=13)	
Median support duration (days)	146 (range 1 to 939)
Discharge with portable device and successfully transplanted	(9/43)

*the majority were supported for more than 90 days with longest patient support for 979 days.

Successful bridge to transplantation varied by diagnosis (75% of patients with dilated cardiomyopathy were bridged to transplant while only 25% with transplant rejection were transplanted.

Abbreviation used: TAH, total artificial heart.

Study 9, 10, 11 Siliopoulos S (2014), Pathak V (2017), Tan SK (2014)

Details

Study type	Case reports
Study population and number	**n=3** 1 64 year old male patient with a 70 cc Syncardia TAH as a BTT for refractory cardiogenic shock as a result of ischaemic cardiomyopathy. 1 52 year old male patient with decompensated heart failure, renal failure, congested liver failure, respiratory failure and biventricular failure underwent TAH and ECMO decannulation. 1 60 year old man with nonischaemic cardiomyopathy implanted with a Syncardia TAH as a bridge to transplantation. Patient underwent dental extractions prior to TAH implantation.
Conflict of interest/source of funding	None

Key efficacy and safety findings

Efficacy

Number of patients analysed: **3**

Case 1: Tear of the left ventricle driveline just above the driveline air-tube junction

Patient was discharged home after TAH implantation with a portable driver but was readmitted on day 172 due to symptoms of pulmonary congestion and progressive exertion intolerance caused by an air leak at the left ventricular driveline. Radiology showed a small horizontal tear above the connection of the driveline to the air tubes. This driveline defect was repaired by cutting the driveline at the location of the tear and reconnecting the air tubes and switching to a new driver.

Case 2: airway complication of TAH

Platelet transfusions for thrombocytopenia due to liver dysfunction and low dose bivalirudin were given after TAH implantation. Patient developed acute onset hypoxia and increased peak airway pressures between days 14 to 19. Patient experienced sudden onset loss of TAH flows and hypotension. Bronchoscopy revealed diffuse haemorrhage and a large clot at the carina spilling from left to right main bronchus. This caused air trapping through a ball-valve phenomenon allowing air to enter but not to escape. A large blood clot was pulled from the airway through an endoscopic retrieval basket and a bronchial blocker was used to tamponade the bleeding.

Case 3: fatal acanthamoeba encephalitis

Patient developed flaccid paralysis of the left upper extremity on day 2 after TAH implantation. CT of the head showed right medial temporal lobe hypodensity raising the possibility of an infection and was treated for encephalitis and bacterial infection. Repeat CT revealed brain oedema with leftward midline shift and uncal herniation. Patient later developed loss of brainstem reflexes despite medical management and died 5 days after TAH implantation. Autopsy revealed necrosis and haemorrhage of the brain parenchyma with numerous amoebic trophozites and double walled cysts. Morphologic analysis, immunoperoxidase staining and molecular analysis confirmed acanthamoeba encephalitis.

'Possible portals of entry include haematogenous spread from recent dental procedures or placement of the total artificial heart device, pulmonary dissemination from use of contaminated continuous positive pressures (CPAP) machine, and reactivation of prior latent infection'.

Abbreviation used: TAH, total artificial heart.

Efficacy

Survival to transplantation

In a non-randomised prospective comparative study of patients at risk of imminent death from irreversible biventricular heart failure, total artificial heart (TAH) implantation (n=81) was compared with matched historical controls (n=35). The rates of survival to heart transplantation were 79% (95% confidence interval [CI] 68% to 87%) in the TAH group compared with only 46% in the control group ($p<0.001$). The 1-year survival to transplantation rates were 70% (95% CI 63% to 77%) and 31% respectively ($p<0.001$)[1].

In a non-randomised retrospective comparative study (United Network of Organ Sharing [UNOS] database analysis), comparing TAH support with biventricular assisted device (BIVAD) support as a bridge to transplantation (BTT) in adult patients undergoing heart transplantation, device support survival rates were not significantly different between TAH and BIVAD support groups (95% compared with 93% at 30 days and 77% compared with 69% at 1 year, $p=0.8$)[3].

In a non-randomised retrospective comparative study comparing TAH support (n=81) with paracorporeal BIVAD support as a bridge to transplantation (BTT) in 148 adult patients, support survival rates were not significantly different between TAH and BIVAD support groups (76% compared 72% at 30 days and 63% compared 61% at 2 months, 46% compared 53% at 6 months, $p=0.87$)[4].

In a case series of 101 patients at risk of imminent death from irreversible biventricular heart failure and eligible for transplant, survival to transplantation with TAH implantation as a BTT was 68% (69/101)[2].

In a case series of 90 patients with biventricular failure treated by TAH implantation as a BTT, actuarial survival on device was 74±5%, 63±6% and 47±8% at 30, 60 and 180 days after implantation respectively[5].

In a case series of 27 patients with TAH implantation as a BTT, 44% (12/27) patients were discharged home from hospital within a median of 88 days after implantation (range 35 to152 days). Support time between discharge and transplantation was spent out of hospital in 87% of patients[7].

Mean support time to transplantation

In the non-randomised prospective comparative study comparing TAH (n=81) with matched historical controls (n=35), the mean time from entry into study to transplantation or death was 79 days in TAH group compared with only 8.5 days in the control group ($p<0.001$)[1].

In the non-randomised prospective comparative study comparing TAH (n=81) with BIVAD (n=67), the mean time from entry into study to transplantation or

death was 71 days in TAH group compared with 79 days in the BIVAD group (p=0.62)[4].

In the case series of 101 patients with TAH as a BTT, the mean TAH support time was 87 days (median 53 days, range 1 to 441 days). Pump outputs during support were 7 to 9 litres per minute[2].

In the case series of 90 patients with TAH as a BTT, the mean duration of support was 84±102 days[5].

In a case series of 47 patients with TAH support for more than 1 year, the median support time was 554 days (range 365 to 1,374 days)[6].

In the case series of 27 patients with TAH implantation, the median device support time was 44 days (range 35 to 152 days)[7].

Survival after transplantation

In the non-randomised prospective comparative study comparing patients who had TAH implantation (n=81) with matched historical controls (n=35), the survival rates at 1 and 5 years after transplantation in the TAH group were 86% and 64% compared with 69% and 34% in the control group respectively[1].

In the non-randomised retrospective comparative study (UNOS database analysis), comparing TAH support with BIVAD support, survival rates after transplantation were 88% compared with 93% at 30 days, 78% compared with 83% at 1 year and 67% compared with 73% at 3 years respectively (p=0.06)[3]. Cox regression analysis shows that TAH is not associated with a worse post-transplant survival (p=0.1)[3].

In the non-randomised comparative study of 148 patients, survival rates after transplantation in the TAH group (n=51) and paracorporeal BIVAD group (n=39) were 77% compared with 76% at 1 year, 72% compared with 70% at 3 years and 70% compared with 58% at 5 years and showed no difference(p=0.60)[4].

In the case series of 101 patients with TAH implantation, survival after transplantation at 1, 5 and 10 years was 76.8%, 60.5% and 41.2% respectively[2].

In the case series of 90 patients with TAH implantation, actuarial survival rates after transplantation were 78±6%, 71±6% and 63±8% at 1, 5 and 8 years respectively[5].

In the case series of 27 patients with TAH implantation, survival after transplantation (n=12) at a median 20-month follow-up was 91%[7].

Overall survival

In the non-randomised prospective comparative study comparing patients who had TAH implantation (n=81) with matched historical controls (n=35), the overall survival rate at 1 year was 70% (95% CI 63% to77% compared with 31% ($p<0.001$)[1].

In the case series of 101 patients with TAH implantation, the overall survival at 1, 5, 10 and 15 years was 55% (n=56), 43% (n=35), 28% (n=18), and 26% (n=3) respectively[2].

In the case series of 90 patients with TAH implantation, the overall actuarial survival rates after device implantation (patients not censored at time of transplantation) were 73.3±4.7, 50.0±5.3, 45.5±5.3 and 43.8±5.3 at 1 month, 1 year, 3 years and 5 years respectively[5].

Treatment success (defined as alive 30 days after implantation, NYHA class I or II, ambulatory, not dependent on a ventilator and not undergoing dialysis)

In the non-randomised prospective comparative study comparing TAH (n=81) with matched historical controls (n=35), treatment success was achieved in 69% patients who had TAH compared with 37% of the controls ($p=0.002$)[1].

Haemodynamic and other outcomes

In the non-randomised prospective comparative study comparing patients who had TAH implantation (n=81) with matched historical controls (n=35), haemodynamic status improved after TAH implantation with a sustained increase in the cardiac index from baseline 1.9 to 3.2 litres/minute/square metre body surface area, mean systolic arterial pressure rose from 93 to 122 mmHg, mean central venous pressure fell from 20 to 14 mmHg, the organ perfusion pressure rose from 49 to 68 mmHg. Renal and hepatic function and the levels of blood urea nitrogen, creatinine, bilirubin, and liver enzymes returned to normal within 3 weeks. Other laboratory values such as electrolyte levels, platelet count, and the white blood cell count also returned to normal at 3 to 4 weeks[1].

Quality of life

In the non-randomised prospective comparative study comparing patients with TAH implantation (n=81) with matched historical controls (n=35), quality of life in TAH group improved significantly: 75% of patients were out of bed 1 week after implantation and mobility (defined as ability to walk more than 100 feet) was seen in 60.5% patients (method of measurement not reported)[1].

In the case series of 27 patients with TAH implantation, the quality of life results for 12 patients at home (measured using a modified ED-5D defined by INTERMACS) show that only 1 young patient was able to return to school. Patients and families reported the console's noise as bothersome[7].

Safety

Deaths

In a non-randomised retrospective comparative study (UNOS database analysis), rates of deaths were not significantly different between total artificial heart (TAH) and biventricular assisted device (BIVAD) groups (22% compared with 45%, p=0.7) while on support (64 compared with 111, p=0.9) after transplantation. The causes of death while on device support (infection, multi-organ failure, stroke or haemorrhage) and after heart transplantation (acute rejection, infection, cardiac arrest, multi-organ failure and stroke) for both groups were also not significantly different[3].

Rates of death before transplantation were 21% (17/81) in the TAH group compared with 54% (19/35) in the control group in a non-randomised prospective comparative study of 130 patients (no statistical analysis presented). Causes of the 17 deaths before transplantation in the TAH group were multi-organ failure, (7), procedural or technical complications (in 4), bleeding (2), sepsis (2), congestive heart failure (1) and pulmonary oedema (1). In the same group after transplantation, there were 6 deaths (graft failure in 3, sepsis in 1, procedural or technical complication in 1 and multi-organ failure in 1)[1].

Rates of deaths in the non-randomised retrospective comparative study of 148 patients were not significantly different between TAH and BIVAD groups while on support (30% compared with 26%, p=0.87) [4].

Deaths during hospitalisation (at a median duration of 26 days of circulatory support) were reported in 56% (15/27) of patients in the case series of 27 patients with TAH implantation. The most frequent cause of death was multi-organ failure (47% [12/27], 2 were related sepsis), bleeding complications (n=1), mesenteric ischaemia (n=1) and cerebrovascular event (n=1). No deaths were reported between discharge and transplant[7].

Deaths were reported in 32% (32/101) of patients in a case series of 101 patients with TAH implantation; 70% of deaths were within the first 14 days. Causes of deaths were multi-organ failure (13), pneumonia or pulmonary oedema (6), sepsis (5), neurologic injury (4, including 1 stroke, 1 hypoxic damage from hypotension and 2 intracranial haemorrhage), pancreatic abscess (1), small intestinal ischaemia (1), disseminated intravascular coagulopathy (1) and disseminated coccidiodomycosis (1)[2].

Deaths were reported in 39% (35/90) of patients while on device support after a mean of 62±107 days in a case series of 90 patients with TAH implantation as a BTT. Causes of death are multiple-organ dysfunction syndrome (19% [17/90]), haemorrhagic or ischaemic stroke (9% [8/90]), bleeding (4% [3/90]), infection (4% [3/90]), gastrointestinal complication (n=1), device failure (n=1) and unknown reasons[5].

Deaths were reported in 25% (12/47) patients while on support within a median time of 525 days [range 381 to 971 days]) in a case series of 47 patients supported with TAH for more than 1 year[6]. Causes of death were sepsis leading to multiple organ failure in 5, device failure in 2 and mediastinitis in 1.

Bleeding

There were 102 bleeding events in 62% (59/95) patients in the TAH group in the non-randomised prospective comparative study of 130 patients. Of these events, 50% occurred during TAH implantation and were mainly tamponade or mediastinal bleeding (needed surgery and blood transfusion) within 21 days. Two patients died from bleeding: 1 during TAH implantation and 1 during heart transplantation)[1].

Bleeding (from various sites) at a mean of 4.2 days was reported in 43% (43/101) of patients in the case series of 101 patients. Reoperations for haemorrhage (mediastinal explorations) were done in 25% (25/101) of patients[2].

The surgical revision rate for bleeding or haematoma was significantly lower in the TAH group than the BIVAD group during support in the non-randomised comparative study (23% [17/81] compared with 42% [28/67] respectively; p=0.03)[4].

Surgical re-exploration for bleeding, haematoma or infection was reported in 39% (35/90) patients while on device support in the case series of 90 patients with TAH implantation[5].

Haemorrhagic events (at a median time of 249 days) were reported in 14% (7/47) of patients in the case series of 47 patients with TAH support for more than 1 year. These included cerebral haemorrhage in 3, subarachnoid haemorrhage in 2 and gastrointestinal bleeding in 2[6].

Bleeding events (mediastinal bleeding or atrial tamponade needing surgery first month after implantation) were reported in 41% (11/27) patients in the case series of 27 patients[7].

Device malfunction and fitting complications

Nineteen device malfunction events were reported in 17% (16/95) of patients in the TAH group in the non-randomised prospective comparative study. One patient died because of perforation in one of the layers of the device's left ventricular diaphragm on day 124[1].

Fitting complications were reported in 5% (5/95) of patients in the TAH group in the same study. In 3 of these patients, the device was repositioned in repeat surgery; 2 patients died as a result of poor fitting[1].

Device failure was reported in 10% (5/47) of patients in the case series of 47 patients with TAH support for more than 1 year. Two events were caused by membrane rupture leading to death; 3 events were nonfatal causing air hole in the driveline in 1, membrane rupture in 1 and lower pump output in1[6].

Device malfunction (technical problems with alarm and computer monitoring system needing console change) was reported in 1 patient during hospitalisation in the case series of 27 patients. Malfunctions were reported in 25% (3/12) of patients discharged home with TAH. In 2 patients an air leak occurred on the driveline to the ventricle and was sealed with a silicone band. In another patient alarm triggering was caused by auricular compression during some movements (stretching and yawning) and the patient was advised to avoid them[7].

Renal failure

The renal failure rate was significantly higher in the TAH support group than the BIVAD support group before (24% [52/212] compared with 10% [35/366], p<0.0001) and after transplantation (26% [56/212] compared with 14% [49/366], p=0.0001) in the non-randomised retrospective comparative study (UNOS database analysis)[3].

Renal failure (needing postoperative renal replacement therapy) was reported in 64% (30/47) patients in the case series of 47 patients with TAH support for more than 1 year. Recovery of renal function occurred in 73% (22/47) patients but therapy continued in 17% (8/47) patients[6].

Infection rate

Infection rate after implantation was significantly lower in the TAH support group on the transplant wait list than the BIVAD support group (22% [46/212] compared with 28% [104/366], p=0.005) in the non-randomised retrospective comparative study (UNOS database analysis)[3].

There were 172 infections reported (7 in blood, 50 respiratory, 5 mediastinal, 28 genitourinary, 12 gastrointestinal, 17 driveline and 6 in catheters) in 77% (73/95) patients in the TAH group in the non-randomised prospective comparative study. Infections contributed to death in 7 patients and delayed transplantation in 5 patients. Of the infections after TAH implantation, 62% occurred during the first 28 days[1].

Infections (more commonly in the lungs and urinary tract) were reported in 64% (64/101) patients in the case series of 101 patients. 50% of these occurred in the first 30 days. Three had clinical mediastinitis but all were treated[2].

Rates of postoperative mediastinitis (TAH 12% [9/81] compared with BIVAD 5% [3/67]; p=0.14) or driveline infections (TAH 1 compared with BIVAD 2, p=0.61) were similar in both groups during support in the non-randomised comparative study[4].

Mediastinitis was reported in 14% (13/90) patients while on device support in the case series of 90 patients with TAH implantation[5].

Driveline infections (superficial in 11, mediastinitis in 2) were reported in 27% (13/47) patients in the case series of 47 patients with TAH for more than 1 year. Five patients died of sepsis with multi-organ failure and 1 died due to mediastinitis. Systemic infections (treated with antibiotics) were reported in 53% (23/47) of patients. Wound infections were reported in 4% (2/47) of patients. [6]

Major infections (needing readmission) were reported in 58% (7/12) of patients discharged home with TAH in the case series of 27 patients. These include driveline infections in 3 and mediastinitis in 4 patients at a median time 90 days. 2 of them were reoperated[7].

Neurologic events

Neurologic events (stroke in 10, transient ischaemic attack in 4, anoxic encephalopathy in 5, metabolic encephalopathy in 1, seizure in 4 and syncope in 1) were reported in 27% (26/95) patients in the TAH group in the non-randomised prospective comparative study. In 6 cases transplantation was delayed[1].

Neurologic events were reported in 16% (16/101) of patients in the case series of 101 patients. Strokes were reported in 8% (8/101) of patients (5 events occurred by 9 days and 3 thereafter). Peripheral emboli (1 at celiac artery, spleen 2, superior mesenteric artery 1, kidney 2, retina 2) were reported in 8% (8/101) of patients, 3 events occurred at less than 7 days and 5 at 38 to 286 days. Four of these patients died[2].

Strokes rates were not significantly different between the TAH and BIVAD groups during support in the non-randomised prospective comparative study of 148 patients (TAH 12% [9/81] compared with BIVAD 24% [16/67], p=0.08)[4].

Strokes were reported in 10% (9/90) of patients while on device support in the case series of 90 patients with TAH implantation[5].

Thromboembolic events (at a median time of 500 days) were reported in 19% (9/47) of patients in the case series of 47 patients with TAH support for more than 1 year. 6 had a transient ischaemic attack and 3 suffered a major cerebrovascular accident with hemiparesis or aphasia[6].

Technical or procedural problems

Eleven technical or procedural problems (obstruction of the mechanical tricuspid valve of the TAH because of migration of central venous catheter) occurred in 3% (3/95) patients in the TAH group in the non-randomised prospective comparative study. This caused death in 1 patient[1].

Catheter entrapment of a central line in the tricuspid valve (leading to brain damage from cardiac arrest) was reported in 2 patients in the case series of 101 patients with TAH implantation. Both these patients had irreversible brain damage from device arrest and died[2].

Reduced cardiac index

Reduced cardiac index (to less than 2 litres/min/square metre for 4 hours or more during first 11 days) associated with 8 events was reported in 9% (9/95) patients in the TAH group in the non-randomised prospective comparative study. These events included fitting problem (1), hypovolaemia (4), pneumothorax (1), tamponade (1) and catheter entrapment (1) and device malfunction (1)[1].

Other events

There were 27 reduced blood pressure events reported in 19% (18/95) of patients in the non-randomised prospective comparative study. This caused death in 2 patients. The study also reported haemolysis in 4% (4/95) of patients, hepatic dysfunction in 37% (35/95) of patients, peripheral thromboembolism in 14% (13/95) of patients, respiratory dysfunction in 36% (34/95) of patients and renal dysfunction in 31% (29/95) of patients[1].

Delayed sternal closure (at a median time 4 days) was reported in 23% (11/47) of patients in the case series of 47 patients with TAH support for more than 1 year[6].

Tear of the left ventricle driveline just above the left ventricular driveline air-tube junction (leading to progressive exertion intolerance and pulmonary congestion) was reported in a case report of 1 patient implanted with a TAH as a BTT for refractory cardiogenic shock as a result of ischaemic cardiomyopathy. This driveline defect was repaired by cutting the driveline at the location of the tear and reconnecting the air tubes and switching to a new driver[9].

Airway complication of TAH due to a large blood clot at the carina spilling from left to right main bronchus (leading to acute hypoxia, increased peak airway pressures, sudden loss of TAH flows and hypotension) was reported in a case report of 1 patient. This caused air trapping through a ball-valve phenomenon allowing air to enter but not to escape. The clot was pulled out from the airway through an endoscopic retrieval basket and a bronchial blocker was used to tamponade the bleeding[10].

Fatal infection was reported in a case report of 1 patient implanted with a TAH. Patient developed flaccid paralysis of the left upper extremity, brain oedema and loss of brainstem reflexes. Patient died after 5 days despite medical management. Autopsy revealed necrosis and haemorrhage of the brain parenchyma with numerous amoebic trophozites and double walled cysts. Morphologic analysis, immunoperoxidase staining and molecular analysis confirmed acanthamoeba species[11].

Validity and generalisability of the studies

- There are no randomised controlled trials comparing total artificial heart (TAH) with left ventricular assist devices (LVADs).
- Three small non-randomised comparative studies compared TAH with biventricular assist devices (BIVADs) or historical controls (no TAH implantation).
- Studies were mainly retrospective.
- One study included patients who had TAH support for more than 1 year.
- Evidence is mainly from 1 device (Syncardia) and its direct predecessors.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Implantation of a left ventricular assist device for destination therapy in people ineligible for heart transplantation. NICE interventional procedure guidance 516 (2015). Available from http://www.nice.org.uk/guidance IPG516
- Short-term circulatory support with left ventricular assist devices as a bridge to cardiac transplantation or recovery. NICE Interventional Procedure Guidance 177 (2006). Available from https://www.nice.org.uk/guidance/ipg177

NICE guidelines

- Chronic heart failure in adults: management. NICE clinical guideline 108 (2010). Available from http://www.nice.org.uk/guidance/NG108
- Chronic heart failure (2017) NICE Pathway
- Chronic heart failure in adults (2011) NICE quality standard 9

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Three Specialist Advisor Questionnaires for artificial heart implantation as a bridge to transplantation for end-stage refractory biventricular heart failure were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme was unable to gather patient commentary for this procedure.

Company engagement

A structured information request was sent to 4 companies who manufacture a potentially relevant device for use in this procedure. NICE did not receive any submissions.

Issues for consideration by IPAC

- IPAC to consider amending the title as 'total artificial heart implantation as a bridge to transplantation for end-stage refractory biventricular heart failure'.
- SynCardia TAH is the only commercially available total artificial heart (TAH) as a bridge to transplantation that has a CE mark and was approved by the United States Food and Drug Administration (FDA) in 2004. The SynCardia TAH also has FDA approval for destination therapy in the US under the Humanitarian Use Device exemption. There are 2 sizes, 70cc device fits majority of patients with a body surface area of 1.7m^2 and 50cc fits smaller patients with body surface area of 1.2 to 1.7m^2.
- AbioCor and Carmat devices are under development. It is not clear if these products are currently available.

- The UK transplant registry holds data on organ donation and transplantation. Currently, the procedure is only used in very small numbers within transplant centres in Papworth and Harefield hospitals.
- SynCardia has a registry.
- Ongoing trials
  - NCT02962973: European Clinical Evaluation of the Carmat Total Artificial Heart. Primary completion June 2017
  - NCT02459054: Syncardia 50cc TAH-t as a Bridge to Transplant. Study completion date June 2020
  - NCT00614510: SynCardia CardioWest TAH-t Postmarket Surveillance Study. Study completed March 2015 (published)
  - NCT00733447: SynCardia Freedom Driver System Study. Study completed May 2014
  - NCT01919320: SynCardia Companion 2 Driver System Post Approval Study Protocol With INTERMACS™-Based Data Collection. Study completion date July 2016
  - NCT02232659: SynCardia 70cc TAH-t for Destination Therapy (DT) . Study completion date December 2019

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4. Nguyen A, Pozzi M et al (2015). Bridge to transplantation using paracorporeal biventricular assist devices or the syncardia temporary total artificial heart: is there a difference? Journal of Cardiovascular Surgery (56) 3 493-502.
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11. Tan SK, Gajurel K et al (2014). Fatal acanthamoeba encephalitis in a patient with a total artificial heart (syncardia) device. Open Forum Infectious Diseases (1) 2 57.

Appendix A: Additional papers on artificial heart implantation as a bridge to transplantation for end-stage refractory biventricular heart failure

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Allen Y, Collins R et al (2009). Managing the failing heart: total circulatory assist--a case study. Progress in Transplantation (19) 1 13-7.	Case report Syncardia Total Artificial Heart implanted in a patient with end stage heart failure	This case study illustrates the challenges of caring for patients with such a device.	Larger studies with longer follow-up included in table 2.
Anderson E, Jaroszewski D et al (2009). Parallel application of extracorporeal membrane oxygenation and the CardioWest total artificial heart as a bridge to transplant. Annals of Thoracic Surgery (88) 5 1676-8.	Case report N=1 patient with biventricular failure who underwent CardioWest total artificial heart-temporary (SynCardia Inc) implantation with extracorporeal membrane oxygenation.	After respiratory and hemodynamic stabilization, the CardioWest total artificial heart-temporary served as a successful 62-day bridge-to-heart transplantation	ECMO+TAH combined procedure
Anonymous (2002). AbioCor totally implantable artificial heart. How will it impact hospitals? Health Devices (31) 9 332-41.	AbioCor technology overview	Describes the operation of the AbioCor and discusses its likely impact on hospitals if it is approved for marketing. It also discusses ventricular assist devices (VADs), used for permanent cardiac support.	Technology review
Arabia FA (2001). Update on the total artificial heart. Journal of Cardiac Surgery (16) 3 222-7.	Review	Jarvik artificial heart, was used initially as a bridge to heart transplantation (BTT). Currently the CardioWest total artificial heart (TAH) is the only device in clinical use with the intention of bridging patients to heart transplantation. Two new TAHs are being developed.	Review
Arabia F (2015). Biventricular support-total artificial heart. Cardiology (Switzerland) (131) 342.	Review SynCardia TAH.	Mechanical circulatory support with LVADs and total artificial hearts (TAHs) served as a bridge to transplantation (BTT) in patients with severe biventricular failure. The majority of the experience is with the SynCardia TAH. Newer TAH's include the Carmat TAH and BiVACOR TAH. The TAH continues to have an increasing role in the management of advance heart failure.	Review
Arabia, FA, Copeland JG et al (1999). Implantation technique for the CardioWest total artificial heart. Annals of Thoracic Surgery (68) 2 698-704.	CardioWest total artificial heart	A detailed description of the implantation technique is presented to facilitate the use of this technology.	Describes implantation technique.

Arabia FA, Copeland JG et al (1993). Progress on the total artificial heart. Surgical Technology International (2) 251-4.	The CardioWest C-70TM (Symbion, Jarvik J-7TM) and the Penn State Heart as a bridge to cardiac transplantation.	The TAH replaces the ventricles and is anastomosed to the respective atria and great vessels. It utilizes mechanical heart valves for inflow and outflow. It connects to a console via drive lines that pierce the skin. The TAH is pneumatically driven, and a personal computer monitors its function.	Describes implantation technique.
Arabia FA., Copeland JG et al (1997). International experience with the CardioWest total artificial heart as a bridge to heart transplantation. European Journal of Cardio-Thoracic Surgery (11 Suppl) S5-10.	Case series N=79 patients with Idiopathic/dilated cardiomyopathy as the most common etiology followed by ischemic cardiomyopathy. CardioWest total artificial heart (TAH) as a bridge to heart transplantation.	The mean duration of implant was 34 days. A total of 55 patients (70%) were transplanted of which 50 survived (91% of patients transplanted) and were discharged home. 21 patients died while on the device. Multiple organ failure was the major cause of death. There were a total of 255 complications in this group that included reoperation, bleeding, hepatic failure, renal failure, respiratory failure, neurologic events, thromboembolic events, infections, device malfunction, and fit complications.	Larger and more recent studies were included in table 2.
Arabia FA and Moriguchi JD (2014). Machines versus medication for biventricular heart failure: focus on the total artificial heart. Future Cardiology (10) 5 593-609.	Total artificial hearts (TAHs) as a beneficial bridge to transplantation.	The TAH has continued to play a significant role as a bridge to transplantation in patients with biventricular failure and more selected indications that could not be completely helped with left ventricular assist devices. Improved survival with the TAH has resulted in more patients benefiting from this technology.	Review
Arabia F, Moriguchi J et al (2014). Single center experience of total artificial heart as a bridge to heart transplantation. Transplantation (98) 54.	Case series N=19 patients who underwent TAH as a bridge to heart transplantation.	6 -month survival for was 74%. The cause of death included: sepsis (2), stroke (2), and multi-organ dysfunction (1). 3 of 19 (16%) patients went on to heart transplantation and all of them are alive and well. 11 of 19 (58%) patients are still being supported by TAH. 26 episodes of complications occurred in 15 patients during follow up.	Larger and more recent studies were included in table 2.

Arabia F, Kittleson M et al (2016). The largest single center experience with total artificial heart implantation: Characterization of outcome. American Journal of Transplantation (16) 211.	Case series N= 48 heart failure patients (average Intermacs level 1.9 +/- 0.9) who required TAH support.	48 patients underwent TAH implantation with a 72.9% (35/48) 6-month survival and/or transplantation rate. Complications were as follows: 22.9% post-implant stroke, 8.3% post-implant bleeding, 25.0% post-implant GI bleeding, and 6.3% (3/48) post-implant driveline infection. 53.3% (24/48) were discharged home. 12 patients underwent heart transplantation with a 6-month and 12-month survival of 100.0%. No patient developed rejection.	Larger studies included in table 2.
Arabia F, Czer L et al (2015). The selection process for total artificial heart. American Journal of Transplantation (15) no pagination.	Case series N=33 patients who underwent TAH placement Patients were divided according to their Intermacs level at the time of TAH implantation. This included Intermacs 1 (n=13), Intermacs 2 (n=11), and Intermacs >3 (n=9).	There was a significant decrease in survival in the Intermacs 1 group compared to the Intermacs 2 and >3 groups (log-rank p=0.013). There is no significant difference in complications among the 3 groups. Patients with severe biventricular heart failure who are Intermacs 1 have significantly lower device success.	Larger studies included in table 2.
Arabia FA, Copeland JG et al (1999). CardioWest total artificial heart: a retrospective controlled study. Artificial Organs (23) 2 204-7.	Retrospective controlled study N=18 TAH CardioWest Versus 16 Intra aortic balloon pump	In Group A, 1 patient died on the TAH, 1 patient died after transplant, and 22 patients reached transplant and were discharged home for a survival rate of 91.7%. In Group B, 10 patients died while waiting for a heart transplant. Of the 8 patients transplanted, 7 survived and were discharged home for a survival rate of 38.9% (p = 0.0003). In summary the CardioWest TAH provided an excellent and successful method of bridging patients to heart transplantation with a reasonable risk.	More recent studies included in table 2.

Arusoglu L, Morshuis M et al. Modified implantation technique of the CardioWest total artificial heart-surgical tipps and tricks.Thoracic and Cardiovascular Surgeon (58) no pagination	CardioWest total artificial heart	Over 130 patients have undergone bridge to transplant with this device at our institution. Patient selection and excellent surgical technique are required for a successful outcome. A detailed description of the implantation technique developed over the last decade is presented.	Describes implantation technique
Barber DA, Hobbs C et al (2003). Anesthetic management for the placement of a fully implantable artificial replacement heart: a case report. AANA Journal (71) 6 431-9.	Case report N=1 patient with end-stage cardiomyopathy Abiocor artificial replacement heart	This article describes the anesthetic management of the recipient of the Abiocor artificial heart with the longest survival time.	Anaesthetic management
Barker LE (1991). The total artificial heart. AACN Clinical Issues in Critical Care Nursing (2) 3 587-97.	Review N=170 TAH as a permanent device or as a bridge to transplant. Symbion J-7-100 TAH (Jarvik-7)	All of these permanent TAH patients suffered from device-related complications including bleeding, infection, and thromboembolic events. More than 70% of these patients being successfully transplanted.	Review
Barnard J and Tsui SS (2012). The total artificial heart in a cardiac replacement therapy programme. British Journal of Hospital Medicine (73) 12 672-6.			Review
Berenson CK and Grosser BI (1984). Total artificial heart implantation. Archives of General Psychiatry (41) 9 910-6.	Case report N=1 Implantation of a total artificial heart.	The criteria for candidate selection, the preoperative psychiatric evaluation, and operative and postoperative complications, mental status over the period of his survival, post-mortem pathologic findings are reviewed.	Larger studies included in table 2.
Brocks Y, Schoenbrodt M et al (2012). Case report:Neuropsychological therapy for patient with a total artificial heart. Thoracic and Cardiovascular Surgeon (60) no pagination.	Case report n-1 patient with an ischemic cardiomyopathy and cardiogenic shock Total artificial heart-CardioWest TM TAH as a bridge to transplant.	Acute ischemic attacks, and subacute strokes diagnosed. Neuropsychological therapy focused on psychological illness and the realization of life dependency on the TAH, helplessness and anxiety about the future. The patient's perceived self-control, which is an indicator for quality of life in MCS patients, was strengthened by neuropsychological diagnostics and therapy.	Larger studies included in table 2.

Broecker L, Zombolas T et al (1990). The total artificial heart - a bridge to transplantation. Journal of Extra-Corporeal Technology (22) 2 79-84.		Discussion includes the training procedure, operation and management of Canada's first total artificial heart implantation.	Review
Bruce CR, Allen NG et al (2014). Challenges in deactivating a total artificial heart for a patient with capacity. Chest (145) 3 625-631.	Case report		Larger studies included in table 2.
Burns GL (1993). Infections associated with implanted blood pumps. International Journal of Artificial Organs (16) 11 771-6.	Case series N=190 Jarvik-7 and Jarvik 7-70 (Symbion-7 and Symbion 7-70) total artificial hearts (TAH) implanted.	Of the 190 patients implanted with these devices, 133 went on to cardiac transplantation and 68 of the transplanted patients are alive. Complications associated with the use of the TAH have included postoperative hemorrhage, thrombosis with thromboembolism and infection. The incidence of infection in the patients implanted with the TAH has declined-significantly since initial clinical use and is now near 30%. Staphylococcus epidermidis and Pseudomonas aeruginosa are the most commonly pathogens isolated from these devices.	Safety event reported in papers included in table 2.
Bunnell K, Voils S et al (2011). Antimicrobial prophylaxis and infection following total artificial heart implantation. Critical Care Medicine (39) 67 2011.	45 patients mainly with a nonischemic cardiomyopathy (82%). who have received a TAH as bridge to transplantation (2006-11)	A five-day prophylactic course of vancomycin, piperacillin-tazobactam, and fluconazole for TAH implantation was associated with a similar rate of overall infection as has been previously reported among TAH recipients.	Safety event reported in papers included in table 2.

Burns GL (1993). Infections associated with implanted blood pumps. International Journal of Artificial Organs (16) 11 771-6.	Review Jarvik-7 and Jarvik 7-70 (Symbion-7 and Symbion 7-70) total artificial hearts	Of the 190 patients implanted with these devices, 133 went on to cardiac transplantation and 68 of the transplanted patients are alive. Complications associated with the use of the TAH have included postoperative hemorrhage, thrombosis with thromboembolism and infection. The incidence of infection in the patients implanted with the TAH has declined-significantly since initial clinical use and is now near 30%. Staphylococcus epidermidis and Pseudomonas aeruginosa are the most commonly pathogens isolated from these devices.	Review
Cabrol C, Gandjbakhch I et al (1992). Total artificial heart as a bridge for transplantation. Cuore (9) 5 461-466.			No abstract
Cabrol C, Gandjbakhch I et al (1989). Current problems in cardiac transplantation. Biomedicine & Pharmacotherapy (43) 2 87-92.	Case series N=34 patients in acute irreversible cardiac failure and who cannot have a transplant in time. Implanted a total artificial heart (TAH) type JARVIK 7	There has been no mechanical failure, hemolysis or thrombo-embolism and only one right ventricular device malposition; 20 patients died before transplantation, 13 were successfully transplanted, 1 is still on the artificial heart. Heart transplantation, and TAH used as a bridge to transplantation are now an accepted therapeutic means for irreversibly cardiac failure in selected patients.	Larger and more recent studies included in table 2.
Cabrol C, Solis E et al (1989). Orthotopic transpantation after implantation of a Jarvik 7 total artificial heart. Journal of Thoracic and Cardiovascular Surgery (97) 3 342-350.	Case series N=33 Orthotopic transpantation after implantation of a Jarvik 7 total artificial heart as abridge to transplantation.	12 patients underwent cardiac transplantation. Another patient is still being supported with the total artificial heart 90 days after implantation. The other 20 patients died during mechanical support because their condition could not be stabilized for transplantation, despite blood flow restoration. Transplantation was performed only when the patient's condition was stable.	More recent studies included in table 2.

Carpentier A., Latremouille C et al (2015). First clinical use of a bioprosthetic total artificial heart: report of two cases. Lancet (386) 10003 1556-63.	CARMAT TAH Case series N=2 patients admitted to hospital who were at imminent risk of death, having irreversible biventricular failure, and not eligible for heart transplantation.	Both patients were extubated within the first 12 postoperative hours and had a rapid recovery of their respiratory and circulatory functions as well as a normal mental status. Patient 1 presented with a tamponade on day 23 requiring re-intervention. Postoperative bleeding disorders prompted anticoagulant discontinuation. The C-TAH functioned well with a cardiac output of 4.8-5.8 L/min. On day 74, the patient died due to a device failure. Autopsy did not detect any relevant thrombus formation within the bioprosthesis nor the different organs, despite a 50-day anticoagulant-free period. Patient 2 experienced a transient period of renal failure and a pericardial effusion requiring drainage, but otherwise uneventful postoperative course. He was discharged from the hospital on day 150 after surgery with a wearable system without technical assistance. After 4 months at home, the patient suffered low cardiac output. A change of C-TAH was attempted but the patient died of multiorgan failure.	Safety events reported in table 2.
Cios Tj, Salamanca-Padilla Y and Guvakov D (2017). An anti-coagulation conundrum: implantation of total artificial heart in a patient with heparin-induced thrombocytopenia type II. American journal of case reports (18) 294-298.	Case report N=1 patient underwent SynCardia Total Artificial Heart (TAH) implantation following a recent left ventricular assist device (LVAD) placement and type II Heparin-induced thrombocytopenia (HIT).	The patient was receiving argatroban for type II HIT with anuric renal failure, and developed a thrombus which occluded the inflow cannula of the LVAD. Based on a published study and after establishing consensus with the surgical, anesthesiology, perfusion, and hematology teams, tirofiban was used as an antiplatelet agent to inhibit the platelet aggregation induced by heparin, and heparin was ultimately used as the anticoagulant for cardiopulmonary bypass.	Larger studies included in table 2.

Cohn WE, Timms DL and Frazier OH (2015). Total artificial hearts: past, present, and future. Nature Reviews Cardiology (12) 10 609-17.	Review	Early total artificial hearts mimicked the pumping action of the native heart. These positive-displacement pumps could provide adequate haemodynamic support and maintain the human circulation for short periods, but large size and limited durability adversely affected recipients' quality of life. The importance of pulsatile circulation remains unclear.	Review
Cook JA, Shah KB, Quader MA et al (2015). The total artificial heart. Journal of Thoracic Disease (7) 12 2172-80.	Review	The history, indications, surgical implantation, post device management, outcomes, complications, and future direction of the TAH are discussed in this review.	Review
Copeland J (2010). Out-of-hospital total artificial heart patients: bridge to transplantation. Texas Heart Institute Journal (37) 6 654-5.			No abstract
Copeland JG (2013). SynCardia Total Artificial Heart: update and future. Texas Heart Institute Journal (40) 5 587-8.	Review	Worldwide, there have been 114 implants of the CardioWest TAH with 72 transplanted (63%) and 66 discharged (58% of total and 92% of those transplanted). Implant times have been as long as 186 days. Given the efficacy and durability of the device and the potential of portability, the future for out of hospital living with this device appears more realistic than ever.	Review

Copeland, J., Copeland, H et al (2013). Results with an anticoagulation protocol in 99 SynCardia total artificial heart recipients. ASAIO Journal (59) 3 216-20.	Case series N=99	After the second post-implant day in patients who were free of endo-device infection (97 patients), the embolic stroke incidence was 0.08 per patient year. This included 23.6 patient years of device support. There were no spontaneous hemorrhagic strokes. 2 patients had endo-device infections and both had strokes. Postimplantation bleeding was seen in 20% of patients. All but 2 of these were within the first postoperative week. In all, 4% of patients had gastrointestinal bleeding. We did not observe heparin-induced thrombocytopenia in any patient.	Similar studies included in table 2.
Copeland JG (1998). Current status and future directions for a total artificial heart with a past. Artificial Organs (22) 11 998-1001 Nov.	Review	Worldwide there have been 114 implants of the CardioWest TAH with 72 transplanted and 66 discharged. Implant times have been 196 days. The future for out of hospital living appears realistic.	Review
Copeland JG (2000). Mechanical assist device; my choice: the CardioWest total artificial heart. Transplantation Proceedings (32) 7 1523-4.			No abstract
Copeland JG, Arabia FA et al (2003). Total artificial hearts: bridge to transplantation. Cardiology Clinics (21) 1 101-13.		The CardioWest TAH has come nearly full circle. It was first used as a destination device. It has since been used as a bridge to transplantation in nearly 200 patients as the Jarvik-7/Symbion TAH.	Review

Copeland JG, Levinson MM and Smith R (1986). The total artificial heart as a bridge to transplantation. A report of two cases. Journal of the American Medical Association (256) 21 2991-2995.	Case report N=2 Jarvik-7 device	In 1 patient unapproved device on an emergency basis, failed after transplantation because of severe pulmonary edema and Pseudomonas pneumonia and the apparent transmission of a Pseudomonas infection from donor to recipient. The second experience, using a Jarvik-7 device, led to stable support for nine days with one major complication, a reversible neurologic deficit with no associated computed tomographic scan abnormality. This patient survived cardiac transplantation and, after being successfully treated for complications, has made a full recovery and returned to full-time work.	
Copeland JG, Smith RG et al (2008). Risk factor analysis for bridge to transplantation with the CardioWest total artificial heart. Annals of Thoracic Surgery (85) 5 1639-44.	N=81 patients CardioWest total artificial heart, as a bridge to transplantation Results were compared with all recent risk factor analyses for other devices.	Risk factors for bridge to transplantation with the CardioWest total artificial heart are different from those reported for left ventricular assist devices. Recognition of these risk factor differences may facilitate appropriate device selection.	Larger and more recent studies included in table 2.
Cabrol C, Gandjbakhch I et al (1988). Total artificial heart as a bridge for transplantation: La Pitie 1986 to 1987. Journal of Heart Transplantation (7) 1 12-17.	Case series N=15 patients with acute irreversible heart failure Jarvik 7 TAH implanted.	Mechanical circulatory support lasted from 1 to 26 days. There was no mechanical failure, no hemolysis, no thromboembolism, and only two cases of right ventricular device malpositions; seven patients died before transplantation, three from infection and four from multiple organ failure; eight had successful transplantations, and six remain well. The Jarvik-7 total artificial heart appeared in our experience to be a safe device, easy to drive, offering the best conditions to these acutely ill patients while they waited for a heart transplantation.	More recent studies included in table 2.

Copeland JG, Arabia FA et al (1998). The CardioWest total artificial heart bridge to transplantation: 1993 to 1996 national trial. Annals of Thoracic Surgery (66) 5 1662-9.	Matched controlled study N=27 patients with end stage heart disease implanted with CardioWest total artificial heart compared with 18 matched retrospective control patients	Of the implant patients, 25 (93%) received a transplant, 24 (89% of the total, 96% of those transplanted) were discharged and are currently surviving. In the control group, 10 patients died awaiting transplantation, 8 received a transplant, and 7 were discharged with 6 surviving (p = 0.00001). All adverse events were documented with respect to time. Thirteen serious adverse events occurred, 11 of which occurred in the 2 patients that died during implant. When compared with the series of matched retrospective controls, a significant improvement in survival was found in the CardioWest implant group.	More recent studies included in table 2.
Copeland H. and Copeland J (2012). Experience with total artificial heart bridge to transplantation in 15 women. Journal of Heart and Lung Transplantation (31) 4 SUPPL. 1 S269.	Case series 15 women (mean 38) who had body surface areas ranging from 1.55 to 2.13 (1.82 mean) cardiomyopathy: dilated in 5, peri-partum in 3, ischemic in 2, hypertrophic in 1, and valvular in 1. Also there were 2 with congenital heart disease and 1 failure to wean from bypass. All were in cardiogenic shock with 1 on cardiopulmonary bypass, one on a BiVAD, 1 on an intra-aortic balloon pump, 5 with cardiac arrests, and 12 were Intermacs 1 and 3 Intermacs 2 pre-implantation. CardioWest (SynCardia) 70 ml ventricles implanted.	The durations of implantation ranged from 1 to 440 days (mean 114). Ten (67%) survived to transplantation and 9 (60%) have survived a minimum of 2 years with 8 currently living 2 to 13 years post-transplantation. There were no fit problems. Causes of death on device support included: neurologic problems in 3, catheter entrapment of the tricuspid valve in 1, and pulmonary edema in 1. Adverse events included: stroke in 1 (minimal residual aphasia), takeback for hemorrhage 2, graft failure in1, TIA in 1, and subdural hemorrhage in 1 (no residual).	Larger studies included in table 2.

Copeland JG., Arabia FA et al (1999). Arizona experience with CardioWest Total Artificial Heart bridge to transplantation. Annals of Thoracic Surgery (68) 2 756-60.	Case series (prospective) N=24 patients CardioWest Total Artificial Heart as bridge to transplantation.	Four patients died while on device support. Nineteen of 23 patients (83%) were transplanted. All 19 survived long term. One patient remains on CardioWest Total Artificial Heart support 6 weeks after implant. There was one stroke on the day of transplantation. There was a second stroke on the day of implantation. Neither stroke caused significant residual deficits. Both were in close relationship to an operative procedure. There were no serious device-related infections.	More recent studies included in table 2.
Copeland JG, Smith RG, Arabia FA et al (2004). Total artificial heart bridge to transplantation: a 9-year experience with 62 patients. Journal of Heart & Lung Transplantation (23) 7 823-31.	Case series (retrospective) N=62 patients with biventricular heart failure. CardioWest TAH implanted between 1993-2002 Follow-up: 9 years	Mortality in this group from the time of implantation until transplantation was 23%. Causes of death during device support included multi-organ failure (6), sepsis (3), and valve entrapment (2). Forty-eight patients underwent transplantation (77%). Forty-two survived to hospital discharge (68% of the total, 88% of those undergoing transplantation). Adverse events included bleeding (20%), device malfunction (5%), fit complications (3%), mediastinal infections (5%), visceral embolus (1.6%), and stroke during support (1.6%). The linearized stroke rate was 0.068 events per patient-year. 68% of critically ill transplant candidates for whom medical therapy failed were bridged to transplantation with the CardioWest TAH and survived long-term. Most deaths that occurred during device support were related to pre-implant problems. Infection and stroke were rare events. Therefore, we recommend the CardioWest TAH as the biventricular bridge-to-transplant device of choice.	More recent studies included in table 2.

Demiselle J, Besson V et al (2016). Total Artificial Heart and Chronic Haemodialysis: A Possible Bridge to Transplantation? Blood Purification (42) 4 301-303.	Case report 51-year-old man who was treated with conventional hemodialysis (HD) while on support with TAH.	The patient underwent HD while on TAH support during 14 months. He benefited from conventional HD, 6 sessions per week. HD sessions were well tolerated, and patient's condition and quality of life improved significantly. The main difficulty was to maintain red blood cell level because of chronic hemolysis due to TAH, which required repetitive blood transfusions, resulting in a high rate of human leukocyte antigen sensitization. Unfortunately, the patient died of mesenteric ischemia due to anticoagulation under dosing.	Safety event covered in table 2.
Dimitriou, Alexandros Merkourios, Dapunt et al (2016). Liver failure in total artificial heart therapy. Journal of Thoracic Disease (8) 7 1546-9.	Case series N=31 patients received a Syncardia Total Artificial Heart	Liver associated mortality in normal liver function, ALF and CH cases was 0%, 20% (P=0.03) and 44.4% (P=0.0008) respectively. 1/17 (5.8%) patients with a normal liver function developed an ALF, 4/5 (80%) patients with an ALF experienced a markedly improvement of hepatic function and 6/9 (66.6%) patients with CH a significant deterioration. TAH therapy results in recovery of hepatic function in ALF cases.	Safety event covered in table.
Dowling RD, Gray Jr LA et al (2004). Initial experience with the AbioCor Implantable Replacement Heart System. Journal of Thoracic and Cardiovascular Surgery (127) 1 131-141.	Case series N=7 Abicor	The initial clinical experience suggests that the AbioCor might be effective therapy in patients with advanced biventricular failure. There have been no significant device malfunctions. Two of these patients have been discharged from the hospital.	Recent studies included in table 2.

Dunseth C. and Firchau DJ (2016). Total artificial heart: An autopsy case series. Laboratory Investigation (96) 6A.	Case series 10 year retrospective review of an autopsy database N=3 SynCardia TAH cases	At autopsy, all cases had intact anastomotic sites, and no thrombi were identified in the TAH device. One case had infarcts of the liver, kidneys and spleen, as well as gastrointestinal ischemia; this patient died due to multi-organ failure complicating the TAH transplant and underlying heart failure. The second case died of acute Cryptococcal, Enterococcal and Escherichia coli pericarditis/mediastinitis and had purulent material surrounding the TAH with involvement of mediastinal soft tissues and chest wall. The third case died of complications of ischemic bowel related to underlying angiodysplasia of a branch of the right colic artery and had a right lower quadrant abscess, which cultured positive for Enterococcus and Candida glabrata; complications of the TAH contributed to the patient's death. The survival after TAH ranged from 13 to 182 days. Two patients died directly from complications of heart failure and TAH surgery. In the third case, complications of heart failure and TAH surgery did not directly cause death but significantly contributed to death.	Autopsy results

El-Banayosy A, Arusoglu L et al (2005). ardioWest total artificial heart: Bad Oeynhausen experience. Annals of Thoracic Surgery (80) 2 548-52.	Case series N=42 patients in persistent cardiogenic shock CardioWest total artificial heart (TAH) implanted	Duration of support was 1 to 291 days. Eleven patients (26%) underwent successful transplantation; 9 of them could be discharged home. Twenty-two patients died under support, 21 of them from multiple organ failure and 1 patient from a technical problem. Nine patients are still on the device, 4 of them at home after the original CardioWest console was replaced by the Berlin Heart EXCOR driver (Berlin Heart, Berlin, Germany). Exceptional results were achieved in patients with cardiogenic shock after cardiac surgery or after acute myocardial infarction.	Larger and more recent studies included in table 2.
Emery RW, Joyce LD et al (1992). Experience with the symbion total artificial heart as a bridge to transplantation. Annals of Thoracic Surgery (53) 2 282-8.	Case series N=9 patients underwent bridging to transplantation using a Symbion J-7-70 total artificial heart.	The Symbion J-7-70 total artificial heart is an effective device for total circulatory support in patients with end-stage cardiogenic shock when an organ donor is not available. Organ system failure and infection before implantation may persist into the transplantation period resulting in long-term complications, increased mortality, and prolonged hospital stay; therefore, early implantation of the device when indicated should be applied.	Larger and more recent studies included in table 2.
Ferng AS, Oliva, I et al (2016). Translation of First North American 50 and 70 cc Total Artificial Heart Virtual and Clinical Implantations: Utility of 3D Computed Tomography to Test Fit Devices. Artif Organs Nov 10.	Case series N=3 patients who have undergone successful 50 and 70 cc TAH implantation with complete closure of the chest cavity utilizing preoperative "virtual implantation" of different sized devices for surgical planning.	All three patients received clinical implants of the properly sized TAH based on virtual modeling, and their chest cavities were fully closed. This virtual implantation increases our confidence that the selected TAH will better fit within the thoracic cavity allowing for improved surgical outcome. Clinical implantation of the TAHs showed that our virtual modeling was an effective method for determining the correct fit and sizing of 50 and 70 cc TAHs.	Larger studies included in table 2.

Friedline K and Hassinger P (2012). Total artificial heart freedom driver in a patient with end-stage biventricular heart failure. AANA Journal (80) 2 105-12.	Case report 61-year-old man admitted with acute decompensated heart failure, which progressively worsened, eventually requiring implantation of a TAH-t.	Following stabilization, the patient was switched to the Freedom driver. After the patient and his wife proved competence in managing the device, they were able to take several daylong excursions outside the hospital. The patient considered discharge from the hospital while awaiting a transplant but ultimately received a heart transplant while still an inpatient.	Larger studies included in table 2.
Gaykowski R, Taylor KD and Yates WG (1988). Cumulative clinical experience with the Symbion J7 TAH. ASAIO Transactions (34) 3 455-9.	Case series N=92 patients with cardiomyopathy Symbion J7 pneumatic TAH as a bridge to cardiac transplantation 63 patients were transplanted	56% (35/56) patients are currently alive, with most returning home and back to work. Implant duration ranged from 1 to 243 days of support, with an average of 24 days. Postoperative complications observed in a population cohort of 70 patients include bleeding in 44%, infection in 34%, reoperation in 27%, neurologic dysfunction in 13%, and device failure in none. Standardized device explant analysis results indicate a trend in thrombus reduction concurrent with increased investigator experience and improved patient management techniques.	Larger and more recent studies included in table 2.

Glass C and Padera, R (2015). Pathology of the syncardia total artificial heart: A case series. Laboratory Investigation (95) 78A.	SynCardia Total Artificial Heart Reviewed the gross and microscopic findings in five (5) TAHs at the time of explant or autopsy along with clinical information.	The mean age of the patients (all male) was 52.8 years (range 39 to 68), with a median support time of 247 days (range: 127-341 days) on the TAH. Two patients had amyloid heart disease, while one each had valvular heart disease, repaired congenital heart disease and allograft vasculopathy; all had biventricular heart failure as the indication for TAH. Four patients (80%) survived to transplantation. One patient with a TAH died from Klebsiella device infection, pneumonia and sepsis. In four of the five devices, thrombosis was present at the junction of the right and left atrium with the atrial sewing cuff of the TAH on the luminal surface, ranging from 0.6cm to 6.5cm in size along the circumference of the anastomosis. A small laminated thrombus was present in the subpulmonic area in the autopsy case. One patient had a radiologically confirmed cerebrovascular accident on the TAH and one patient had a pulmonary embolism confirmed at autopsy. All atrial cuffs showed near transmural necrosis and mummification, with some viable myocardium in the subendocardial region. There was no evidence of dehiscence in any device. Thrombosis at the atrial-device interface and devitalization of the atrial myocardium were the dominant findings in the TAHs.	Pathologic findings in SynCardia TAHs.

Gajurel K, Tan S et al (2014). Acanthamoeba encephalitis in a patient with a total artificial heart (syncardia device). Transplantation (98) 422.	Case report N=1 A 60 year old male with a worsening cardiomyopathy (NYHA class 4) was admitted for a Total Syncardia Device as a bridge to cardiac transplantation.	2 days later he was found to have flaccid paralysis of left upper extremity and altered mental status requiring mechanical ventilation and vasopressor support. CT of the head showed right medial temporal lobe hypodensity without enhancement in an atypical location for ischemia- raising the possibility of an infection. The patient was started on acyclovir for presumed HSV encephalitis. Repeat CT head revealed increased brain edema and 8 mm leftward midline shift with uncal herniation. The patient's condition continued to deteriorate. He was eventually transitioned to comfort care and died 5 days after the Syncardia placement. Autopsy revealed necrotic lesions in the brain with amoebic trophozoites (20-22 microns with a single nucleus and a prominent nucleolus) and double walled cysts. Immunoperoxidase staining confirmed Acanthamoeba species. Conclusion: The source of infection remains under investigation. The possibilities include dissemination from a cutaneous source on his forearm, the implanted device, and, reactivation of a latent infection. This is the first case report of Acanthamoeba encephalitis in a patient with Total Syncardia Device.	Multiple publication of an article included in table 2.
Griffith BP, Hardesty RL et al (1987). Temporary use of the Jarvik-7 total artificial heart before transplantation. New England Journal of Medicine (316) 3 130-4.	Case series N=6 Jarvik-7 total artificial heart was implanted into 6 moribund patients in an attempt to test its potential as a bridge from almost certain death to cardiac transplantation.	The results of this trial indicate that in properly selected cases, direct benefit to the patient can be obtained when the Jarvik-7 artificial heart is used as a bridge to transplantation.	Larger and more recent studies included in table 2.

Ghodsizad Ali, Koerner, Michael M et al (2016). Total Artificial Heart Implantation Blood Pressure Management as Resolving Treatment for Massive Hemolysis following Total Artificial Heart Implantation. Heart Surgery Forum (19) 5 E229.	Case report N=1 patient with non-ischemic dilated cardiomyopathy with advanced cardiogenic shock. Syncardia TAH 70cc implanted	Postoperatively patient developed renal failure and required continuous haemodialysis. Patient also had hypertension and extensive anaemia. After treatment patient recovered.	Larger and more recent studies included in table 2.
Grimm JC, Sciortino CM et al (2016). Outcomes in Patients Bridged With Univentricular and Biventricular Devices in the Modern Era of Heart Transplantation. Annals of Thoracic Surgery (102) 1 102-8.	Comparative case series N= 4,177 adult patients in UNOS database. 3,457 (20.4%) left ventricular assist device [LVAD]), 575 (3.4%) biventricular assist device [BiVAD], and 145 (0.9%) biventricular or total artificial heart [TAH]) device. Unconditional and conditional survivals were compared with the Kaplan-Meier method. Cox proportional hazards regression models were constructed to determine the risk-adjusted influence of support type on death.	Unadjusted 30-day, 1-year, and 5-year estimated survival was greater in LVAD patients than in the BiVAD and TAH cohorts. After risk-adjustment, BiVAD and TAH were associated with an increased risk of death at all time points. Unadjusted and adjusted 5-year survival, conditional on 1-year survival, was worse, however, only in TAH patients. Patients with biventricular failure bridged to transplantation with a TAH or BiVAD experienced worse short- and long-term survival compared with those with an LVAD. This difference is most likely due to an increase in early death and depends on the type of BiVAD device implanted.	Survival outcomes comparing TAH and BiVAD are reported in table 2.
Gomez CK and Hobbs S (2016). Total Artificial Heart Imaging and Complications: a Pictorial Review. The VAD Journal: the journal of mechanical assisted circulation and heart failure. 16 Aug.	Review on CT imaging modality in early recognition of total artificial heart (TAH) complications.	The aim of this review is to illustrate the TAH components and CT based imaging of TAH complications. Recognition of TAH complications can help to plan for early intervention and therefore improve patient's survival.	Review

Hansen AJ and Copeland JG (2010). Combined heart kidney transplant after CardioWest total artificial heart bridge. Journal of Heart and Lung Transplantation (29) 10 1193-1195.	Case report N=1 adult with end-stage cardiomyopathy and renal failure who was bridged to combined, single-donor HKTx with a CardioWest total artificial heart.	Infectious complications associated with the CardioWest cavity were encountered prior to transplantation. The patient recovered and was discharged 14 days after transplantation. At 4 months post-transplantation, the patient required single-vessel coronary stenting for a high-grade stenosis. At 1 year, he has had no further complications and has excellent function of both transplanted organs. Despite limited availability of same donor organ pairs, patients with combined cardiac and renal failure can be bridged effectively to transplant with the CardioWest total artificial heart.	Larger and more recent studies included in table 2.
Hermsen JL, Smith JW et al (2015). Late Surgical Bleeding Following Total Artificial Heart Implantation. Journal of Cardiac Surgery (30) 10 771-4.	Case series N=10	Ten patients underwent TAH implant. Four patients experienced delayed postoperative bleeding. In three patients the manifestation of bleeding was tamponade and evidenced by TAH decreased cardiac output. In two patients, at postoperative days 31 and 137, there was a partial disruption of the aortic anastomosis along the outer curvature with pseudoaneurysm formation. Both were repaired by primary suture closure, without use of cardiopulmonary bypass. There was no mortality attributable to bleeding.	Larger studies included in table 2.

Hidalgo LF, Shah KB et al (2017). Infections in Patients with a Total Artificial Heart are Common but Rarely Fatal. ASAIO Journal.	Case series N= 32 patients who received a total artificial heart (TAH)	Infections were classified as confirmed or suspected. The mean duration of TAH support was 225 days (range 1 to 1334 days). Of the 32 patients, 4 (12.5%) died and 28 (87.5 %) underwent heart transplantation. Causes of death were pneumonia (n=1), TAH malfunction (n=1), refractory cardiogenic shock (n=1), and respiratory failure (n=1). Seventy documented and 13 suspected infections developed in 25 patients (78%). The most common sources of infection were urinary tract (n=26), respiratory tract (n=18), and bloodstream (n=11). There were 5 pump infections and 2 drive line infections. The number of infections per patient ranged from 0 to 10. Sixteen different pathogens were identified; the most common were: Klebsiella pneumoniae (n=15), coagulase-negative Staphylococci (n=10), Enterococcus species (n=9) and Enterobacter species (n=8). Mortality directly attributable to infection was infrequent.	Infections and complications are reported in table 2.
Hosseinian L, Levin MA et al (2015). Hemodynamic deterioration during extracorporeal membrane oxygenation weaning in a patient with a total artificial heart. Critical Care Medicine (43) 1 e19-22.	Case report N=1 patient with recurrent episodes of ventricular tachycardia requiring emergent total artificial heart and venovenous extracorporeal membrane oxygenation placement. Inferior vena cava compression by a total artificial heart masked for days by the concurrent placement of an extracorporeal membrane oxygenation cannula was reported.	Total artificial heart patients with hemodynamic compromise or reduced device filling, consideration should always be given to venous inflow compression, particularly in those with smaller body surface area.	Larger studies included in table 2.

Jaroszewski DE, Anderson EM et al (2011). The SynCardia freedom driver: a portable driver for discharge home with the total artificial heart. Journal of Heart & Lung Transplantation (30) 7 844-5.	Case report N=1 patient with irreversible cardiogenic shock. Syncardia TAH implanted.	After 865 days support the patient received a dual heart and kidney transplant and is home doing well.	Larger studies included in table 2.
Jaroszewski DE, Pierce CC et al (2009). Simultaneous heart and kidney transplantation after bridging with the CardioWest total artificial heart. Annals of Thoracic Surgery (88) 4 1324-6.	Case report N=1	Successful treatment of a patient having heart and renal failure with the CardioWest (SynCardia Inc, Tucson, AZ) total artificial heart for bridge-to-cardiac transplantation of a heart and kidney reported.	Larger studies included in table 2.
Kalya A, Goel R et al (2011). Impact of syncardia Total Artificial Heart on renal function in patients bridged to heart transplant. American Journal of Transplantation (11) 301.	Case series N=18 patients with biventricular failure who were candidates for HTX were bridged with TAH.	Cr and GFR worsened following TAH in 10 of the 18 patients (56%) requiring dialysis (HD). 7 of these pts (70%) completely recovered renal function and were off HD prior to undergoing successful HTx; 2 underwent heart kidney Tx. 3 of the 18 pts (17%) died (1 on HD) while on TAH support prior to HTx; and 1 still alive on TAH support (800days) awaiting for a suitable donor for HTx only. No obvious pts variables were identified which predicted the need for HD. AH support significantly improved recovery of renal function in 70% of these patients resulting in successful HTx. The overall survival to HTx amongst the pts needing HD was not significantly different compared to the patients who did not need HD. The higher incidence of HD in TAH patients compared to left ventricular assist device patients is probably related to their higher INTERMACS score, indicative of sicker patient population, at the time of TAH implantation.	Larger studies included in table 2

Kalya A, Jaroszewski D et al (2013). Role of total artificial heart in the management of heart transplant rejection and retransplantation: case report and review. Clinical Transplantation (27) 4 E348-50.	Case report and world-wide experience utilizing the SynCardia CardioWest Total Artificial Heart.	Review of world-wide experience for use of TAH-t in this type patient.	Review
Kawabori M, Kurihara C et al (2017). Total artificial heart implantation for biventricular failure due to eosinophilic myocarditis. Journal of Artificial Organs 1-4.	Case report N=1 patient with acute severe biventricular heart failure caused by eosinophilic myocarditis with mural left ventricular apical thrombus implanted with a total artificial heart as a bridge to heart transplant.	The first case reported in the literature describing a patient with acute severe biventricular heart failure caused by eosinophilic myocarditis with mural left ventricular apical thrombus that was successfully treated with implantation of a total artificial heart as a bridge to heart transplant.	Larger studies included in table 2.
Kirklin JK (2015). Advances in mechanical assist devices and artificial hearts for children. Current Opinion in Pediatrics (27) 5 597-603.	Review on application of adult continuous flow pumps to pediatric patients.	Two continuous flow pumps (HVAD and HeartMate II) have been successfully applied in children and adolescents, and the SynCardia total artificial heart has been used in adolescents. New continuous flow devices are entering or poised to enter clinical trials. If approved, these devices will enhance the safety and variety of options for longer-term pediatric support.	Review
Kasirajan V, Tang DG et al (2012). The total artificial heart for biventricular heart failure and beyond. Current Opinion in Cardiology (27) 3 301-7.	Review	TAH is an effective therapeutic option for the treatment of patients dying of heart failure who may not be suitable candidates for left ventricular assist devices.	Review
Khalpey, Zain, Kazui, Toshinobu et al (2016). First North American 50 cc Total Artificial Heart Experience: Conversion from a 70 cc Total Artificial Heart. ASAIO Journal (62) 5 e43-5.	Case report N=1 female with a prior heart transplant diagnoised with chronic rejection and allograft vasculopathy and listed for transplant. Syncardia 70 to 50 cc TAH implanted.	First TAH exchange from a 70 to 50 cc due to fit difficulty. The patient failed to be closed with a 70 cc TAH although she met the fit criteria for 70cc. it was successfully closed with a 50cc TAH. Patient was hemodynamically stable but died of sepsis 6 weeks postoperatively.	Large studies included in table 2.

Kawaguchi AT, Gandjbahch I et al (1990). Liver and kidney function in patients undergoing mechanical circulatory support with Jarvik-7 artificial heart as a bridge to transplantation. Journal of Heart Transplantation (9) 6 631-7.	Case series N=32 Changes in liver and kidney function were reviewed in 32 patients who received a Jarvik-7 total artificial heart (TAH) as a bridge to transplantation.	Although preoperative liver and kidney dysfunction were frequent and severe, they did not correlate with postoperative functional recovery and later transplantation. Recipient body size and initial postoperative urine output were found to be the variables discriminating patients with or without subsequent transplantation. Because liver/kidney failure remained as the leading cause of death, knowledge of the underlying cause of the organ failure would increase the success of TAH as a bridge to transplantation.	Larger studies included in table 2.
Kawaguchi, AT, Cabrol, C et al (1991). Preoperative risk analysis in patients receiving Jarvik-7 artificial heart as a bridge to transplantation. European Journal of Cardio-Thoracic Surgery (5) 10 509-14.	Case series N=37 Implantation of a Jarvik-7 artificial heart as a bridge to transplantation, our 37 attempts were reviewed retrospectively.	Multiple preoperative factors in combination could have successfully predicted the outcome of mechanical support in our experience. These results underscore the importance of patient selection to achieve successful and effective use of the Jarvik-7 as a bridge to heart transplantation.	Larger studies included in table 2.
Kawaguchi, AT, Gandjbakhch, I et al (1990). Factors affecting survival in total artificial heart recipients before transplantation. Circulation (82) 5 Suppl IV322-7.	Case series N=32 recipients of the Jarvik-7 artificial heart was reviewed to identify factors affecting the successful bridge to transplantation.	The results suggest that device fitting as manifested by body size is an important factor affecting major organ recovery and subsequent transplantation in recipients of the Jarvik-7 artificial heart. A paracorporeal device may be advisable for patients with body surface areas of less than 1.8 m2 or who were less than 175 cm in height until an even smaller model with a better fit in the thorax becomes available.	Larger studies included in table 2.

Leprince P, Bonnet N et al (2003). Bridge to transplantation with the Jarvik-7 (CardioWest) total artificial heart: a single-center 15-year experience. Journal of Heart & Lung Transplantation (22) 12 1296-303.	Case series-retrospective N=127 terminal biventricular failure patients bridged to transplantation with total artificial heart (TAH) Jarvik-7 (CardioWest). In Group I patients (78%), had dilated cardiomyopathy, either idiopathic (n = 60) or ischemic (n = 38). The other 29 patients (Group II) had disease of miscellaneous origin.	Duration of support for transplant patients increased after 1997, reaching 2 months for the recent period (5 to 271 days). In Group I, the percentage of transplanted patients increased from 43% before 1993 to 55% between 1993 and 1997, and reached 74% thereafter. The major cause of death was multiorgan failure (67%). The clinical thromboembolic event rate was particularly low with no instance of cerebrovascular accident and 2 transient ischemic attacks. Total bleeding complication rate was 26%, including 2 deaths related to intractable hemorrhage and 2 others related to atrial tamponade. The cumulative experience was 3,606 total implant days with only 1 instance of mechanical dysfunction.	Larger and more recent studies included in table 2.
Lick, Scott D, Tran, Phat L et al (2016). Total Artificial Heart, Augmented by Venovenous Extracorporeal Membrane Oxygenation. ASAIO Journal (62) 4 e35-6.	Case report N=1 patient with nonischemic cardiomyopathy and end stage biventricular failure. SynCardia total artificial heart (TAH) implanted	Shortly after SynCardia total artificial heart (TAH) implant, venovenous extracorporeal membrane oxygenation (ECMO) via a 31 Fr Avalon cannula was used for profound hypoxic lung dysfunction. Immediately after starting ECMO, TAH flow increased by 1.5-2.0L/min, presumably because of augmented TAH filling by the ECMO jet.	TAH+ECMO
Loforte, A, Della Monica, PL and Musumeci, F (2011). Two years and 4 months: a long-term bridge to transplantation with a total artificial heart. Journal of Heart & Lung Transplantation (30) 12 1419.	Case report N=1 patient with refractory end stage biventricular heart failure due to dilative cardiomyopathy. Syncardia TAH implanted.	The first successful implantation beyond 832 days TAH support due to lack of donor organs.	Larger studies included in table 2.

Meyer, A and Slaughter, M.The total artificial heart.	Review on TAH	The Syncardia/CardioWest TAH remains an important and viable option for patients with severe biventricular failure and end organ dysfunction. Overall, a 79% survival rate has been achieved in patients supported with a Syncardia/CardioWest TAH as bridge-to-transplantation. In this review article, a brief history on the evolution of TAH devices, their current use and emerging use of evolving continuous flow VAD technology as chronic biventricular and TAH device systems are presented.	Review
Myers TJ, Robertson, K et al (2003). Continuous flow pumps and total artificial hearts: management issues. Annals of Thoracic Surgery (75) 6 Suppl S79-85.	Case series N=44 Compared the Jarvik 2000 axial-flow pump and the AbioCor TAH	Jarvik 2000 as a bridge to transplantation (n = 34) or destination therapy (n = 11) for an average duration of support of 132.8 days (5 to 853 days). In 30 bridge-to-transplantation cases, 14 patients (47%) have undergone heart transplantation, 5 (17%) continue to be supported with the Jarvik 2000 device, and 11 (37%) have died. Five of 7 patients supported by the AbioCor TAH survived beyond the perioperative period; 4 were ambulatory, 2 were discharged from the hospital, and 1 is at home 13 months after implantation. Anticoagulation therapy and infection management are necessary for both systems.	Larger and more recent studies included in table 2
Murray KD, Myerowitz PD et al (1989). Effect of a total artificial heart on adaptive hormonal responses in humans with end-stage heart failure. ASAIO Transactions (35) 3 229-31.	Case report N=1 patient with end-stage heart failure received a J-7-70 TAH as a bridge to transplantation	The TAH, used in end-stage heart failure, restores normal hemodynamics and compensatory hormonal levels. These hormones can be used as indicators of proper TAH function in such patients.	Larger and more recent studies included in table 2.

Miessau J, Yang Q et al (2015). Veno-venous extracorporeal membrane oxygenation using a double-lumen bi-caval cannula for severe respiratory failure post total artificial heart implantation. Perfusion (United Kingdom) (30) 5 410-414.	Case report N=122-year-old female with post-partum cardiomyopathy and cardiogenic shock Concomitant extracorporeal membrane oxygenation (ECMO) during placement of a total artificial heart (TAH, SynCardia)	During VV ECMO support, adequate flows on both ECMO and TAH were maintained without adverse events. VV ECMO was discontinued once the patient's respiratory failure improved. the patient subsequently developed a profound respiratory acidosis and required VV ECMO for CO2 removal. T The patient was supported for 22 days on VV ECMO and successfully weaned from the ventilator prior to her orthotropic heart transplantation.	Larger studies included in table 2.
Morris RJ (2012). The Syncardia Total Artificial Heart: Implantation Technique. Operative Techniques in Thoracic and Cardiovascular Surgery (17) 2 154-164.	Syncardia total artificial heart		Describes only implantation technique.
Morshuis M, Reiss N, et al (2007). Implantation of CardioWest total artificial heart for irreversible acute myocardial infarction shock. Heart Surgery Forum (10) 4 E251-6.	Case series N=5 CardioWest total artificial heart was implanted in 5 patients in irreversible cardiogenic shock	After implantation all dysfunctional organ systems rapidly recovered in all. 4 of 5 patients underwent successful heart transplantation after a mean support time of 156 days. 1 patient died because of enterocolic necroses caused by an embolic event after termination of dicumarol therapy. Our first experience justify this extensive management in young patients who would otherwise have died within a few hours.	Larger and more recent studies included in table 2. Device obsolete
Mohacsi P and Leprince P (2014).The CARMAT total artificial heart. European Journal of Cardio-Thoracic Surgery (46) 6 933-4.	Review		Review

Muneretto C, Solis E et al (1989). Total artificial heart: survival and complications. Annals of Thoracic Surgery (47) 1 151-7.	Case series N=28 patients TAH (Jarvik 7) as a bridge to transplantation	No clinical thromboembolic complications occurred during implantation. There was no postoperative bleeding requiring operation. Eleven patients underwent successful transplantation, and 1 patient is still on mechanical support. Sepsis and multiple-organ failure were the most important causes of death. All patients receiving the total artificial heart for severe acute rejection after transplantation died of infection. Early implantation of the total artificial heart is advised in younger patients and in older patients with acute cardiac failure. The use of this device should be contraindicated in immunosuppressed patients because of the high risk of infection.	Larger and more recent studies included in table 2.
Muneretto C, Rabago G et al (1990). Mechanical circulatory support as a bridge to transplantation: current status of total artificial heart in 1989 and determinants of survival. Journal of Cardiovascular Surgery (31) 4 486-91.	Case series N=40 TAH (Jarvik 7) as a bridge to transplantation	There was no postoperative bleeding requiring surgery nor were there any clinical episodes of thromboembolic complications. Over a total functioning period greater than 3 years there were no mechanical failures in the driving system but one artificial ventricle had to be replaced because of mechanical dysfunction. Infections and multiple organ failure were the primary causes of morbidity and mortality during mechanical support.	Larger and more recent studies included in table 2

Olsen DB, Long JW and Anderson JL (1997). **T**he total artificial heart: From initial application to therapeutic option. Journal of Interventional Cardiology (10) 5 335-342.	Review focuses on TAH development.	Worldwide clinical application now spans 27 years and includes experience with TAH implantation in 311 patients, with eight different pneumatically driven devices implanted either as permanent devices (N = 5) or as temporary, bridging therapy to transplantation (N = 306). Based on the evolving experience, use of the TAH as a bridge to transplantation in selected patients who are not appropriate for an LVAD has become a viable current therapeutic option. Further TAH development and application is anticipated.	Review
Park SS, Sanders DB et al (2014). Total artificial heart in the pediatric patient with biventricular heart failure. Perfusion (29) 1 82-8 Jan 2014.	Case report N=1 paediatric patient (14-year-old) with dilated cardiomyopathy and severe biventricular heart failure. Total Artificial Heart (TAH-t) (SynCardia) implanted.	The virtual 3D model confirmed appropriate device fit with no evidence of compression to the left pulmonary veins. The postoperative course was complicated by a left lung opacification. The left lung anomalies proved to be atelectasis and improved with aggressive recruitment maneuvers. The patient was supported for 11 days prior to transplantation	Larger studies included in table 2.
Total Artificial Heart: State-of-the-art. Petukhov, D. S., Selishchev, S. V. and Telyshev, D. V. Biomedical Engineering (49) 4 193-196 2015.	Review	Modern variants of total artificial pulsating hearts such as Syncardia, Abiocor, and Carmat are reviewed.	Review

Pifarre R, Sullivan H, et al (1990). Use of the total artificial heart and ventricular assist device as a bridge to transplantation. Journal of Heart Transplantation (9) 6 638-43.	Case series N=18 (15 Jarvik-7 TAH, 3 Symbion VAD) as a bridge to transplantation inpatients awaiting for heart transplantation. The underlying heart conditions were ischemic cardiomyopathy (11), dilated cardiomyopathy (5), giant cell myocarditis (1), and allograft failure (1).	The average duration of mechanical support was 10 days. 17 patients had successful transplants. 1 patient had brain death and did not receive a heart transplant. Of the 17 patients who survived surgery, 2 died within 30 days: o1 at 17 days because of acute rejection, the other at 14 days because of a cerebral vascular event. 15 patients (83%) were long-term survivors. 9 of the supported patients required reoperation because of bleeding after device implantation. There was no mediastinal or incisional infection.	Larger and more recent studies included in table 2.
Prasad A, Ghodsizad A et al (2016). Non-Cardiac Symptoms of Moderate to Severe Hypokalemia in a Patient with a SyncardiaTM Total Artificial Heart. Heart Surgery Forum (19) 1 E12-3.	Case report N=2 patients with SyncardiaTM total artificial heart (TAH)	One complication from aggressive diuresis is hypokalemi. In two separate instances non-cardiac symptoms related to severe hypokalemia occurred. These symptoms included nystagmus in one patient and agitation, tremors, and having an "out-of-body" experience in the other patient. Both these patients had resolution of symptoms with potassium replacement.	Larger studies included in table 2.
Ramy MH, Huma H et al (2017). Patient with a total artificial heart maintained on outpatient dialysis while listed for combined organ transplant, a single center experience. Hemodialysis International. August 2017.	Case report N=1 patient who had an implanted TAH and develop renal failure.	Patient with a TAH and renal failure transitioned successfully to outpatient hemodialysis and maintained for more than 2 years, though he did not survive to transplant.	Larger studies included in table 2.

Rafiei M, Moriguchi J, Kittleson M et al (2017). Does the model for end stage liver disease (meld) score predict outcome in total artificial heart patients? American Journal of Transplantation (17) 648.	Case series N=76 patients were implanted with a TAH device. We sought to determine whether the MELD score can predict outcome in TAH patients. Patients were divided into OPTN MELD level ranges: MELD less than or equal to 10 (Group A, n=12), MELD 11 to 18 (Group B, n=22), MELD 19 to 24 (Group C, n=20), MELD more than 24 (Group D, n=22). The MELD score was calculated for each patient immediately prior to TAH implant using OPTN MELD calculator.	In general, there is a correlation of increasing MELD score to decreasing survival. Particularly, the worse MELD score group (more than 24) had significantly lowest survival. The lowest MELD score has only 12 patients. 8/12 (67%) of deaths in the highest MELD group were due to multi-organ system failure. The MELD score appears to predict patients undergoing TAH who have increased risk for mortality. Further studies with larger population sizes and follow-up are warranted to confirm these results.	Study reports a scoring system to assess and predict mortality in patients with TAH implantation.
Roussel JC, Senage T, et al (2009). CardioWest (Jarvik) total artificial heart: a single-center experience with 42 patients. Annals of Thoracic Surgery VOL 87 PT 1 PP 124-130.	Case series-retrospective N=42 patients awaiting heart transplant. CardioWest (Jarvik) total artificial heart implanted. 1990-2006	Duration of support was 1 to 292 days (mean, 101 days). 12 patients died (28.5%) while receiving device support, and 30 patients (71.5%) underwent transplantation. Actuarial survival rates for the transplanted patients were 90% (n = 25), 81% (n = 14), and 76% (n = 10) at 1, 5, and 10 years, respectively. Causes of death during device support included multiorgan failure in 6 (50%), sepsis in 2, acute respiratory distress syndrome in 2, alveolar hemorrhage in 1, and other cause in 1. There were no device malfunctions that led to patient death. Adverse events included stroke in 3 patients (7%) and infections in 35 patients (85%) during support.	Larger and more recent studies included in table 2.

Reich H, Czer L et al (2015). Total Artificial Heart Bridge to Transplantation for a Patient With Occult Intracardiac Malignancy: Case Report. Transplantation Proceedings (47) 7 2291-4.	Case report A 51-year-old man with refractory heart failure who underwent total artificial heart implantation as a bridge to transplantation with the surprise finding of an isolated deposit of metastatic carcinoid tumor nested within a left ventricular papillary muscle in his explanted heart.	The primary ileal carcinoid tumor was identified and resected completely. After remaining cancer-free for 14 months, he was listed for heart transplantation and was transplanted 2 months later. He is currently 3.5 months out from heart transplantation and doing well, without evidence of recurring malignancy.	Larger studies included in table 2.
Scully MS, Wessman DE et al (2017). Total Artificial Heart Implantation as a Bridge to Heart Transplantation in an Active Duty Service Member With Amyloid Cardiomyopathy. Military Medicine (182) 3 e1858-e1860.	Case report N=1 patient diagnosed with advanced cardiac amyloid who underwent total artificial heart transplant as a bridge to heart transplant and eventual autologous stem cell transplant.	The patient received a total artificial heart as a bridge to orthotopic heart and kidney transplantation and eventual stem cell transplant. He continues to be in remission and has a fair functional capacity without restriction in activities of daily living or moderate exercise.	Larger studies included in table 2.
Shah KB, Thanavaro KL et al (2016). Impact of INTERMACS Profile on Clinical Outcomes for Patients Supported With the Total Artificial Heart. Journal of Cardiac Failure (22) 11 913-920.	Case series (retrospective) N=66 consecutive patients implanted with the TAH (2006-12) and compared outcome by INTERMACS profile.	Survival after TAH implantation at 6 and 12 months was 76% and 71%, respectively. INTERMACS profile 1 patients had decreased 6-month survival on the device compared with those in profiles 2-4 (74% vs 95%, log rank: P=.015). For the 50 patients surviving to heart transplantation, the 1-year posttransplant survival was 82%. There was no difference in 1-year survival when comparing patients in the INTERMACS 1 profile with less severe profiles (79% vs 84%; log rank test P=.7; hazard ratio [confidence interval] 1.3 [0.3-4.8]). Patients implanted with the TAH as INTERMACS profile 1 had reduced survival to transplantation compared with less sick profiles. INTERMACS profile at the time of TAH implantation did not affect 1-year survival after heart transplantation.	Larger studies included in table 2.

Slepian MJ (2011). The SynCardia temporary total artificial heart-evolving clinical role and future status. US Cardiology (8) 1 39-46.	Review SynCardia temporary total artificial heart	The TAH is a complete, robust, pulsatile, biventricular replacement system indicated for use as a bridge to transplantation in cardiac transplant candidates at risk of imminent death from non-reversible biventricular failure. More than 900 TAHs have been implanted to date, with a bridge-to-transplant success rate >79%. Technological advances continue to be imparted to the TAH system including portable driver enhancements, remote monitoring, and next-generation TAH designs.	Review
Spiliopoulos S, Dimitriou AM et al (2015). Expanding Applicability of Total Artificial Heart Therapy: The 50-cc SynCardia Total Artificial Heart. Annals of Thoracic Surgery (100) 3 e55-7.	Case report N=1	Describes the implementation of this technology in a female patient with irreversible cardiogenic shock on the grounds of acute myocardial infarction and chronic ischemic cardiomyopathy.	Larger studies included in table 2.
Spiliopoulos S, Dogan G et al (2013). Veno-venous extracorporeal membrane oxygenation with a bicaval dual-lumen catheter in a SynCardia total artificial heart patient. Journal Of Cardiothoracic Surgery (8) 179.	Case report N=1 SynCardia total artificial heart (TAH) patient.	55 years old male with cardiogenic shock due to an extended myocardial infarction who underwent SynCardia Total Artificial Heart implantation and veno-venous extracorporeal membrane oxygenation with a bicaval dual-lumen cannula for the treatment of adult respiratory distress syndrome	ECMO+TAH combined procedure
Spiliopoulos S, Guersoy D et al (2015). Implantation technique of the 50-cm3 SynCardia Total Artificial Heart: does size make a difference? Multimedia Manual of Cardiothoracic Surgery.	Review Implantation technique of the 50-cm(3) SynCardia Total Artificial Heart	Despite downsizing, implantation technique of the 50-cm(3) SynCardia Total Artificial Heart and settings of the Companion driver remain unchanged.	Review

Smith MC, Arabia F et al (2005). CardioWest total artificial heart in a moribund adolescent with left ventricular thrombi. Annals of Thoracic Surgery (80) 4 1490-2.	Case report N=15 year old boy with Beckers' muscular dystrophy and cardiomyopathy awaiting heart transplantation A paracorporeal biventricular assist device and a CardioWest total artificial heart were implanted as bridge to transplant. He suffered a cardiac arrest and was placed on extracorporeal membrane oxygenator.	Multiple left ventricular thrombi were identified at the time of the ventriculectomy. The patient did well with the total artificial heart was transplanted and discharged home.	Larger and more recent studies included in table 2.
Trubel W, Schima H, Rokitansky A et al (1989). Clinical total artificial heart bridging: Viennese strategy and experiences. Artificial Organs. VOL 13 PT 5 PP 470-5	Case series n=5 deteriorating heart transplant patients Total artificial heart implantation follow-up: 40 days	After TAH implantation, the conditions of all patients improved, organ dysfunctions restored, and 3 patients underwent subsequent heart transplantation. Bridging lasted for 9-12 days. 2 patients had infection and could not undergo transplantation.	Larger and more recent studies included in table 2.
Torregrossa G, Anyanwu A et al (2014). SynCardia: the total artificial heart. Annals of Cardiothoracic Surgery (3) 6 612-20.	Review SynCardia total artificial heart (TAH)	Meticulous hemostasis with double layer sutures, use of Gore-Tex sheets around the TAH and the pericardial cavity, and use of tissue expanders to avoid contraction of pericardial cavity around the device are discussed in detail. Additionally, experience with implantation of TAH in various challenging scenarios, such as patients with a small chest cavity, congenital heart defects, and simultaneous use of extracorporeal membrane oxygenation (ECMO) reported.	Review
Tang DG, Shah KB et al (2014). Implantation of the syncardia total artificial heart. Journal of Visualized Experiments (89) 18 Jul 18.	Review of a case report and results from a medical centre Syncardia total artificial heart	TAH patients face unique risks with regard to renal failure and anaemia. Anaemia following TAH implantation can be profound and persistent. Despite the profound presentation of these sick patients, there is a 79-87% success in bridge to transplantation.	Review

Shah NR, Jaroszewski DE et al (2015). SynCardia portable Freedom Driver a single-center experience with 11 patients. Innovations: Technology and Techniques in Cardiothoracic and Vascular Surgery (10) 3 188-194.	Case series (retrospective) N=11 underwent TAH-t implantation and transfer to portable driver (Freedom driver)	Transfer to portable driver after TAH-t implant was a median of 46 days. 91% (10/11) patients were bridged to transplantation. 1 patient died on support. 45.5% (5/11) patients were discharged home and 5 (45.5%) remained in-patient on the portable driver before transplantation. 4 patients (80%) successfully discharged home required at least 1 hospital readmission. 6 patients (55%) transferred to the portable driver required a return to a main driver console. 2 patients were then returned to the portable driver for bridge to transplantation.	Larger studies included in table 2.
Trochu JN, Roussel JC et al (2015). Exercise tests by a patient supported with the carmat bioprosthetic heart. European Journal of Heart Failure (17) 81.	Case report N=1 Carmat TAH	Exercise tests performed by a patient supported with the Carmat TAH with fixed pump output were well tolerated. The intraventricular right diastolic and left systolic pressures rose during the tests, indicating a compensatory physiological vascular resistance increase in response to higher oxygen demand with fixed cardiac output.	Larger studies included in table 2.
Villa CR and Morales David LS (2017). The Total Artificial Heart in End-Stage Congenital Heart Disease. Frontiers in Physiology (8) 131.	Review	The total artificial heart (TAH), which has right and left sided pumps that can be arranged in a variety of orientations, can accommodate the anatomic variation present in congenital heart disease (CHD) patients. This review provides an overview of the potential use of the TAH in patients with CHD.	Review
Wells D, Villa CR et al (2017). The 50/50 cc Total Artificial Heart Trial: Extending the Benefits of the Total Artificial Heart to Underserved Populations. Seminars in Thoracic & Cardiovascular Surgery Pediatric Cardiac Surgery Annual (20) 16-19 Jan 2017.	Case series N=28 worldwide patients implanted with 50cc Syncardia TAH (with cardiomyopathy (17), post bypass failure (3), congenital heart disease (2), failed LVAD (2), transplant rejection (2) and other (2)). Median BSA 1.7m^2	Fourteen patients (50%) have had a positive outcome to date. Mortality 50% (14/28). Median support time 66 days (range 0-298). Alive on device 29% (8/28). Patients discharged with portable driver and transplanted 21% (6/28).	Larger studies included in table 2.

Yaung J, Arabia FA (2017). Perioperative Care of the Patient With the Total Artificial Heart. Anesthesia and Analgesia no pagination.	Review	This review discusses the history, indications, and perioperative management of the total artificial heart with emphasis on the postoperative concerns.	Review
Youdle J, Penn S et al (2017). Veno-venous extracorporeal membrane oxygenation using an innovative dual-lumen cannula following implantation of a total artificial heart. Perfusion (United Kingdom) (32) 1 81-83.	Case report	53-year-old male patient underwent implantation of a total artificial heart (TAH) for biventricular failure. However, due to the development of post-operative respiratory dysfunction, the patient required ECLS for six days.	

Appendix B: Related NICE guidance for artificial heart implantation as a bridge to transplantation for end-stage refractory biventricular heart failure

Guidance	Recommendations
Interventional procedures	**Implantation of a left ventricular assist device for destination therapy in people ineligible for heart transplantation. NICE interventional procedure guidance 516 (2015).** 1.1 Current evidence on the efficacy and safety of the implantation of a left ventricular assist device for destination therapy in people ineligible for heart transplantation is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit. For people who are eligible for heart transplantation, refer to NICE's interventional procedure guidance on short-term circulatory support with left ventricular assist devices as a bridge to cardiac transplantation or recovery. 1.2 Patient selection should be done by a multidisciplinary team that includes a cardiologist with a specialist interest in heart failure, a cardiothoracic surgeon and a cardiac anaesthetist (see section 1.3). 1.3 Implantation of left ventricular assist devices for destination therapy should be done by surgeons, anaesthetists and intensive care specialists with special training and regular practice in performing this procedure and caring for these patients. Subsequent care should be provided by a multidisciplinary team including staff with the expertise to deal with patients' medical and psychological management, and with the maintenance of their left ventricular assist devices. 1.4 Clinicians should enter details on all patients who have a left ventricular assist device for destination therapy onto the UK Central Cardiac Audit Database. **Short-term circulatory support with left ventricular assist devices as a bridge to cardiac transplantation or recovery. NICE Interventional Procedure Guidance 177 (2006).** 1.1 Limited evidence on the safety and efficacy of short-term circulatory support with left ventricular assist devices (LVADs) as a bridge to cardiac transplantation or recovery appears adequate to support the use of this procedure provided that the normal arrangements are in place for audit and clinical governance. 1.2 Clinicians should ensure that patients fully understand the high complication rates associated with this procedure and that the procedure is a temporary measure. In addition, use of the Institute's information for the public is recommended. 1.3 Publication of further research will be useful, particularly on the use of this procedure in patients with cardiogenic shock following acute myocardial infarction.

NICE guidelines	**Chronic heart failure in adults: management. NICE clinical guideline 108 (2010).** 1.2.3 Invasive procedures *Coronary revascularisation* 1.2.3.1 Coronary revascularisation should not be routinely considered in patients with heart failure due to systolic left ventricular impairment, unless they have refractory angina. [2003] *Cardiac transplantation* 1.2.3.2 Specialist referral for transplantation should be considered in patients with severe refractory symptoms or refractory cardiogenic shock. [2003] *Cardiac resynchonisation therapy* Refer to 'Cardiac resynchronisation therapy for the treatment of heart failure'. (NICE technology appraisal guidance 120 [2007]). Please refer to the NICE website for updates on the review status of this appraisal. *Implantable cardioverter defibrillators* Refer to 'Implantable cardioverter defibrillators for arrhythmias' (NICE technology appraisal guidance 95 [2006]). Please refer to the NICE website for updates on the review status of this appraisal.

Appendix C: Literature search for artificial heart implantation as a bridge to transplantation for end-stage refractory biventricular heart failure

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane)	22/08/2017	Issue 8 of 12, August 2017
Cochrane Central Database of Controlled Trials - CENTRAL	22/08/2017	Issue 7 of 12, July 2017
HTA database (Cochrane)	22/08/2017	Issue 4 of 4, October 2016
MEDLINE (Ovid)	22/08/2017	1946 to August Week 2 2017
MEDLINE In-Process (Ovid)	22/08/2017	August 21, 2017
EMBASE (Ovid)	22/08/2017	1974 to 2017 Week 34
PubMed	22/08/2017	n/a
JournalTOCS	22/08/2017	n/a

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1 Heart failure/

2 ((heart or cardiac) adj4 fail*).tw.

3 ((advanc* or (acute adj4 decompensat*) or (end adj4 stage) or (irreversible* adj4 biventric*) or progress*) adj4 (heart adj4 failure*)).tw.

4 Myocardial infarction/

5 (acute adj4 myocardial adj4 infarction).tw.

6 MI.tw.

7 Cardiomyopathies/

8 cardiomyopath*.tw.

9 Shock, Cardiogenic/

10 (cardiogenic adj4 shock*).tw.

11 Ventricular dysfunction/

12 ((Biventric* or bi-ventric* or ventric*) adj4 (dysfunction or fail* or defect*)).tw.

13 Heart defects, Congenital/

14 (Congenital adj4 (heart* or cardiac*) adj4 (defect* or disease* or malform* or disfigur* or abnormal* or mutat* or deform*)).tw.

15 or/1-14

16 Heart, Artificial/

17 (total* or tempor*).tw.

18 16 and 17

19 ((total* or tempor*) adj4 artificial adj4 heart*).tw.

20 TAH*.tw.

21 or/18-20

22 15 and 21

23 Heart Transplantation/

24 ((heart or ventric* or cardiac) adj4 (transplant* or graft* or replac*)).tw.

25 (destination* adj4 (therap* or treat*)).tw.

26 Heart-Assist devices/

27 ((heart* or ventric* or cardiac* or biventric* or bi-ventric*) adj4 (assist* or aid*) adj4 (device* or apparat* or equipment* or machin*)).tw.

28 bridg*.tw.

29 or/23-28

30 22 and 29

31 SynCardia*.tw.

32 CardioWest*.tw.

33 Jarvik-7*.tw.

34 AbioCor*.tw.

35 (CARMAT* or C-TAH* or CW-TAH*).tw.

36 or/30-35

37 animals/ not humans/

38 36 not 37

39 limit 38 to english language

40 limit 39 to ed=20170301-20170831