Review Article

Minimally invasive aortic valve replacement in high risk patient groups

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Abstract: Minimally invasive aortic valve replacement (AVR) aims to preserve the sternal integrity and improve postoperative outcomes. In low risk patients, this technique can be achieved with comparable mortality to the conventional approach and there is evidence of possible reduction in intensive care and hospital length of stay, transfusion requirement, renal dysfunction, improved respiratory function and increased patient satisfaction. In this review, we aim to asses if these benefits can be transferred to the high risk patient groups. We therefore, discuss the available evidence for the following high risk groups: elderly patients, re-operative surgery, poor lung function, pulmonary hypertension, obesity, concomitant procedures and high risk score cohorts.

Keywords: Minimally invasive surgical procedures; aortic valve; elderly; reoperation; left ventricular (LV) dysfunction

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Introduction

Aortic valve replacement (AVR) via median sternotomy remains the standard treatment for aortic valvular disease. However, the development of minimally invasive approaches in general surgery has driven the adoption of lesser invasive techniques within the field of cardiac surgery. Historically, Cosgrove and Cohn were the first clinicians to pioneer smaller incisions for both mitral and aortic procedures (1). Despite longer cardiopulmonary bypass (CPB) times compared to conventional surgery (1-12), preservation of the sternal integrity and minimisation of dissection had been advocated to improve the cosmetic result, reduce bleeding, provide better respiratory function, yield shorter hospital stays and therefore lower costs and improved patient satisfaction. A large meta-analysis by Phan *et al.* demonstrated that minimally invasive AVR (mini-AVR) is also associated with a reduced incidence of renal failure and has comparable mortality and morbidity to conventional surgery (13). The above advantages could prove significant in the "high risk" cohorts such as elderly patients, re-operative surgery, poor respiratory status, pulmonary hypertension, renal dysfunction or poor left ventricular (LV) function (14,15). Hence, the current review focuses on the outcomes following mini-AVR in the above high risk groups. Although the definition of minimally invasive approach to the aortic valve remains a matter of debate, the present review discusses the open approaches, performed via a small incision (e.g., not a full sternotomy), therefore we do not refer to the trans-catheter aortic valve implantation (TAVI) (16). We included all the studies where the aortic valve was approached via a minimally invasive approach including: the various types of partial sternotomy, mini-thoracotomy or port-access approach.

Methods

A thorough literature search was conducted in PubMed and Embase databases, using the following search string: "(minimally invasive OR mini OR mini OR minimal access OR partial sternotomy OR hemi-sternotomy OR anterior thoracotomy OR parasternal OR transverse sternotomy) AND (aortic valve) AND (replacement OR surgery OR insertion) AND (high risk OR elderly OR old age OR elderly OR left ventricular failure OR left ventricular dysfunction OR renal failure OR chronic kidney disease OR renal dysfunction OR chronic lung disease OR chronic obstructive pulmonary disease OR re-do OR reoperative OR resternotomy OR reintervention OR pulmonary hypertension)". Further articles were identified by cross reference check from the articles identified by our search.

Mini-AVR in elderly patients

The increase in the life expectancy has resulted in more aortic valve surgery being performed in the elderly population (17). With an increasing prevalence with age, calcific aortic stenosis (AS) is the main valvular disease in the octogenarians with a predicted requirement for approximately 3,500 AVRs per year in England (17,18). Certainly, conventional AVR (CAVR), performed via full midline sternotomy, remains the definitive treatment and yields excellent results (19). However, elderly patients are less able to cope with the stress of surgery due to a reduced vital organ reserve and various associated comorbidities (18). Several retrospective studies, reported outcomes of mini-AVR versus CAVR in the elderly population (*Table 1*).

Grossi *et al.* (20) compared the outcomes of 166 patients (mean age of 77.5 years) undergoing CAVR, with 56 patients (mean age 76 years) undergoing mini-AVR port access technique. There was no difference in hospital mortality. However, the mini-AVR group had a lower incidence of sepsis and wound complications, decreased fresh frozen plasma transfusion requirement and shorter length of hospital stay.

A prospective study by Sharony *et al.* (21) matched 189 patients undergoing mini-AVR and 189 patients undergoing CAVR via sternotomy. All patients were aged over 65, with 28% being octogenarians. The two cohorts had similar hospital mortalities and similar rates of: re-intervention, stroke, wound infection, gastro-intestinal complications, new renal failure and respiratory failure. The CPB times were similar but the mini-AVR group had a shorter hospital stay and more patients were discharged to their own home.

The same group (22) reported results of two propensity-matched cohorts, 233 patients each, aged >80 years, undergoing either mini-AVR or CAVR. Hospital mortality and perioperative morbidity was similar in both groups. However, a greater proportion of mini-AVR patients had a reduced length of hospital stay and were discharged home rather than transferred to a rehabilitation facility. In the multivariate analyses, the presence of severe atheromatous aortic diseases and need for urgent operation increased the risk of hospital mortality.

ElBardissi *et al.* (23) reported outcomes of 249 consecutive mini-AVRs in octogenarians patients that were at a prohibitive high risk (median EuroSCORE of 11% and STS score 10.5%) and were considered candidates for TAVI. Interestingly, the high cardiac surgery risk scores were not predictive of operative mortality which proved to be only 3%. Also, the perioperative morbidity was low: stroke 4%, renal failure requiring dialysis 1%, cardiac arrest 1%, sepsis 1% and pulmonary embolism 1%. The long-term survival of up to 10 years did not differ from a low risk, age and gender matched population.

A retrospective review of consecutive heart operations in patients aged 75 or above, conducted by Lamelas *et al.* (24), identified 58 patients that underwent mini-AVR performed by mini-thoracotomy and compared them with a cohort of 43 patients that underwent CAVR. The composite of mortality and morbidity was significantly lower in the minimally invasive group. This was due to a lower incidence of renal failure, reduced intubation time, less wound infection and fewer deaths. Furthermore, the intensive care unit (ICU) length of stay and total length of hospital stay were lower in the mini-AVR group.

In a small series of 58 isolated mini-AVR performed via a mini sternotomy in patients with median age of 76, Alassar *et al.* (25) reported no operative mortality and no late mortality at 6 months. There was one reoperation for bleeding, no pacemaker insertion and no wound infections. The CPB times were acceptable and the ICU mean stay was approximately 2 days and the hospital mean stay was 6 days. Similarly, a larger retrospective study by Krishna *et al.* (26) on 255 consecutive mini-AVRs, done via mini-right thoracotomy in octogenarians, reported acceptable morbidity and mortality rates.

Santarpino *et al.* (27) allocated 66 patients undergoing sutureless mini-AVR to two age groups: age ≥80 years (25 patients) and age ≤80 (41 patients). The outcomes in terms

Table 1 Mini-AVR in elderly patients

Author, date	Study type and level of evidence	Patient groups and study design	Minimal access approach	Outcomes	Comments	Author's conclusions
Grossi *et al.*, 1998 (20)	Retrospective, level III	259 patients (mean age 77.5 years) had standard sternotomy (SS); 111 patients minimally invasive port access mean age 76.0 years); 166 (64.1%) patients had aortic valve replacement via SS while 56 (50.4%) had AVR done via minimally invasive port access approach	Port access	Hospital mortality: 9.7% (25/259) in conventional group and 7.2% (8/111) in mini-AVR group (P=0.50); mini-AVR: significantly lowered incidence of sepsis or wound complications (1.8% *vs.* 7.7%; P=0.027), required less fresh frozen plasma transfusion, (median 1 *vs.* 2 units; P=0.04) and had a shorter stay (11.6 *vs.* 17.6 days; P=0.001)	Mixed series of aortic and mitral surgery; mitral surgery was performed significantly more often in the minimally invasive group (49.5% *vs.* 35.9%; P≤0 .001)	Mini-port AVR yields excellent results in elderly and is associated significantly less plasma transfusion, fewer postoperative complications, and shorter length of hospital stay
Sharony *et al.*, 2003 (21)	Prospective, propensity matched, level III	189 mini-AVR patients were matched with 189 CAVR patients by age, ventricular function, valvular pathology, urgency of operation, diabetes, previous cardiac surgery, renal disease, and history of stroke. All patients were above 80 years	Right anterior mini-thoracotomy	No difference in hospital mortality (6.9%) and freedom from postoperative morbidity, mini-AVR versus CAVR (82.5% versus 81.5%, P=0.79); in multivariate analysis: urgent procedures (OR 3.97; P=0.03), congestive heart failure (OR 3.94; P=0.03), and ejection fraction 30% (OR 4.16; P=0.03) were predictors of hospital mortality and prolonged length of stay was associated with age (P=0.05), stroke (OR 3.5, P=0.001), CHF (OR 2.2, P=0.004), and SS (OR 2.3, P=0.002). Mini-AVR patients were discharged home (52.6% versus 38.6%, P=0.03) rather than to rehabilitation facilities; no difference in survival at 3 years		Mini-AVR is safe in elderly patients, with morbidity and mortality comparable to SS and is associated with shorter stay and more patient discharged home
Sharony *et al.*, 2004 (22)	Retrospective, propensity matched level III	2 matched cohorts of 233 mini-AVR and 223 CAVR. Matching variables included left ventricular ejection fraction <30%, previous myocardial infarction, CHF, previous cardiac surgery, renal insufficiency, age, gender, COPD, peripheral vascular disease, previous stroke or carotid disease, urgent/emergent operation, valvular pathophysiology, and atheromatous aortic disease	Right anterior mini-thoracotomy	Hospital mortality mini-AVR *vs.* SS groups: 5.6% versus 7.3% (P=0.45) and morbidity: 13.3% versus 14.2% (P=0.79); multivariable analysis: mortality associated with: severe atheromatous aortic disease (P=0.001), COPD (P=0.002), and urgent operation (P=0.02); freedom major perioperative morbidity (86.7% versus 85.8%; P=0.79); median length of stay was shorter with mini-AVR (6 versus 8 days; P<0.001); greater proportion of mini-AVR patients than SS patients was discharged home rather than sent to rehabilitation facilities or nursing homes (65.7% versus 52.9%; P=0.05)		Mini-AVR results in comparable mortality or morbidity to CAVR and is associated with shorter stay and more patients being discharged home

Table 1 (*continued*)

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Author, date	Study type and level of evidence	Patient groups and study design	Minimal access approach	Outcomes	Comments	Author's conclusions
Elbardissi *et al.*, 2011 (23)	Retrospective, level III	249 mini-AVR in octogenarians [84±3 (range 80–95)], EuroSCORE) and Society of STS score used for risk stratification	upper sternotomy	Operative mortality was 3% (n=8/249); median modified EuroSCORE (11%; IQR, 6–14) and STS score (10.5%; IQR, 7–17) were not predictive of 30-day mortality (EuroSCORE C-index =0.527, P=0.074, STS score C-index =0.67, P=0.18); long-term survival after minimally invasive aortic valve replacement at 1, 5, and 10 years was 93%, 77%, and 56%, respectively with no significant difference in long-term survival compared with that of a US age- and gender-matched population (SMR, 1.01; 95% CI, 0.76–1.37; P=0.88); in multivariate analysis: increasing age (HR, 1.10; P=0.08) and severe COPD (HR, 2.52; P<0.007) were significant predictors of survival		Excellent outcomes after mini-AVR with long-term survival that is no different than that of an age and gender-matched US population
Lamelas *et al.*, 2011 (24)	Retrospective, level III	Consecutive patients age >75 years: 119 mini-AVR versus 84 who had CAVR	Right anterior mini-thoracotomy	Median postoperative length (mini-AVR *vs.* SS groups) =7 (IQR 6 to 10) *vs.* 12 (IQR 9 to 20) days, P<0.001; ICU length of stay (mini-AVR *vs.* SS groups) was 52 (IQR 44 to 93) versus 119 (IQR 57 to 193) h, P<0.001; in-hospital mortality (mini-AVR *vs.* SS groups): 2 (1.7%) *vs.* 8 (9.5%, P=0.01 and composite postoperative morbidity and mortality occurred in 25 (21%) *vs.* 38 (45.2%), P<0.001; difference in in the composite of mortality or morbidity driven by: acute renal failure, 1 (0.8%) *vs.* 14 (16.7%), P<0.001; intubation (hours): 23 (19.3%) *vs.* 32 (38.1%), P=0.003; wound infections: 1 (0.8%) *vs.* 5 (6%), P=0.034; and death 8 (9.5) *vs.* 2 (1.7), P=0.01; CPB, IQR, (mini-AVR *vs.* SS groups): 118 (67–186) *vs.* 86 (39–268), P<0.001; AoX time; 84 (40–154) *vs.* 61 (25–156), P<0.001		Lower morbidity and mortality of mini-AVR in elderly compared to SS

Table 1 (*continued*)

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Author, date	Study type and level of evidence	Patient groups and study design	Minimal access approach	Outcomes	Comments	Author's conclusions
Alassar *et al.*, 2013 (25)	Retrospective, level III	58 patients (76.1±9.4 years) who had mini-aVR	Hemi-upper sternotomy	AoX: 54.6±6.3 min, CPB time: 71.2±11.3 min, time of surgery: 154.1±26.8 min, re-operation for bleeding: 1 case (1.7%); no strokes or pacemaker implantations needed, mean ventilation time =4.5 h; mean ICU stay =2 days; mean length of hospital stay =6 days; no mortality, sternal	Single arm study	Mini-AVR safe in the elderly
Krishna *et al.*, 2014 (26)	Retrospective, level III	Mini-AVR in 255 consecutive patients with a mean age 83.5±3 years	Right anterior mini-thoracotomy	4 patients (1.6%) had cerebrovascular accidents, 38 (14.9%) prolonged ventilation, 4 (1.6%) reoperation for bleeding, and 8 (3.1%) acute kidney injury; median intensive care unit length of stay =48.5 h (IQR 27–92 h) and the postoperative length of stay =7 days (IQR 5–9 days); 30-day mortality =3.1% (n=8), combined end point of morbidity and mortality 19.2% (n=49), all-cause mortality at 1 year =6.7% and at 3 years =10.2%	Single arm study; 3 cases were re-do	Mini-AVR can be performed safely in the elderly with acceptable outcomes
Santarpino *et al.*, 2013 (27)	Prospective, level III	66 patients mini-AVR with sutureless Perceval S bioprosthesis allocated to age group ≥80 years (n=25) or age group <80 years (n=41)		Length of intensive care unit stay was similar in both groups (age ≥80 *vs.* <80): 1.9±0.8 *vs.* 2.5±1.4 days, P=0.061; in-hospital mortality occurred in only one patient aged ≥80 years; transient cerebral ischemic similar in age ≥80 *vs.* <80, P=0.59; no difference in pacemaker implantation (1.5 versus 3%; P=0.68), 2 patients age ≥80 versus 1 patient age <80 died during a mean follow-up was 13.9±7.4 months, no significant differences between groups in SF-36 questionnaire answers	Mean EuroSCORE greater in age group ≥80 years (12.3±7.1 *vs.* 7.7±3.8, P=0.002)	Mini-AVR results comparable for in patients aged ≥80 years were comparable to those of younger patients

Table 1 (*continued*)

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Author, date	Study type and level of evidence	Patient groups and study design	Minimal access approach	Outcomes	Comments	Author's conclusions
Gilmanov *et al.*, 2015 (17)	Retrospective, propensity matched level III	Patients aged 80 years, propensity score matching: 100 mini-AVR *vs.* 100 SS	Right anterior mini-thoracotomy	No difference in operative times, mini-AVR patients had a larger prosthesis (P<0.001) and were more likely to receive a sutureless valve (P<0.001); shorter time for extubation (P<0.001) and shorter hospital length of stay (P=0.005) for mini-AVR, no difference in transient ischaemic attack (P=0.47), more postoperative strokes in CAVR [0 *vs.* 4 (4.0%) (P=0.043)], no differences in pacemaker (P=0.47) or new-onset of atrial fibrillation (P=0.28), no difference in operative mortality (P=0.68), mini-AVR more likely to be discharged straight to home (P=0.031), similar survival rates (mini-AVR *vs.* SS) at 5 years (80% *vs.* 81%, P=0.37), minimally invasive approach no impact on survival (P=0.38)	The median follow-up duration was longer in the SS group (59 *vs.* 24 months, P<0.001)	Mini-AVR safely performed in patients aged ≥80 years and associated with lower postoperative stroke incidence, earlier extubation and shorter hospital stay
Moscarelli *et al.*, 2016 (28)	Meta-analysis of non-randomized studies, level II	1,347 patients (675 conventional standard sternotomy and 672 minimally invasive valve surgery)	Right anterior mini-thoracotomy or upper sternotomy	Comparable early mortality to standard sternotomy (OR 0.79, 95% CI, 0.40–1.56, P=0.50) with no heterogeneity (P=0.13); mini-AVR associated with reduced intubation time (OR 0.48, 95% CI, 0.30–0.78) and reduced post-operative length of stay (WMD −2.91, 95% CI, −3.09–−2.74, P<0.00001); CPB times and (WMD 24.29, 95% CI, 22.97–25.61, P<0.00001 and AoX times (WMD 8.61, 95% CI, 7.61–9.61, P<0.00001) were longer for minimally access valve surgery	Pooled outcomes for aortic and mitral valve surgery; subgroup analysis demonstrated statistically significant reduced post-operative length of stay for both minimally invasive aortic and mitral surgery	Mini-AVR or minimally invasive mitral surgery associated with longer CPB and AoX times but shorter intubation and lengths of stay

Abbreviations: AVR, aortic valve replacement; mini-AVR, minimally invasive aortic valve replacement; SS, standard sternotomy; CAVR, conventional aortic valve replacement via median sternotomy; CPB, cardiopulmonary bypass; AoX, aortic cross clamp; IQR, interquartile range; ICU, intensive care unit; AKI, acute kidney injury; PPM, permanent pacemaker; AF, atrial fibrillation; OR, odds ratio; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; SMR, standardized mortality ratio; CI, confidence interval; HR, hazard ratio; EuroSCORE, European System for Cardiac Operative Risk Evaluation; STS, Society of Thoracic Surgeons; WMD, weighted mean difference.

of in-hospital mortality, stroke, pacemaker implantation, survival (mean follow-up of approximately 14 months) were not different. A health and wellbeing survey questionnaire was conducted with no differences reported between the groups.

Gilmanov *et al.* (17) compared two propensity matched groups of isolated mini-AVRs performed via a right anterior thoracotomy (100 patients) versus a full sternotomy (100 patients). Patients were aged 80 years or above. The main findings of the study were reduced stroke incidence, earlier extubation time and shorter hospital stay, favouring the minimally invasive group. Both the in-hospital mortality and long-term survival at 5 years were similar. The rate of postoperative atrial fibrillation (AF) and permanent pacemaker (PPM) insertion rates did not differ.

Moscarelli *et al.* (28) conducted a systematic review of non-randomised studies of 340 elderly patients (mean population age above 75) who received mini-AVR versus CAVR in 343 patients. They found comparable mortality to full sternotomy, significantly reduced postoperative length of stay, no significant difference in CPB and aortic cross-clamp (AoX) times.

Re-do minimally invasive aortic valve surgery

Several studies investigated the potential benefits of minimally invasive surgery in re-operative aortic valve surgery. Theoretically, a smaller incision would reduce the dissection area resulting in less bleeding from adhesion lysis and less risk of damaging patent coronary grafts. Furthermore, preservation of the sternal integrity in such high-risk patients improves the respiratory function and patients have shown to have shorter hospital stay (29-31) (*Table 2*).

In 2000, Byrne *et al.* (32) reported 34 re-do AVR via partial sternotomy. Sixty-two percent of the patients had previous coronary artery bypass grafting (CABG) while 41% had previous valve surgery. There were no intraoperative deaths and no conversions to full sternotomy. The early mortality was 5.9% due to arrhythmia in one case and a large stroke in the other case. There were no reoperations for bleeding and the median lengths of stays in ICU and hospital were 1 and 7 days respectively.

Sharony *et al.* (33) reported the outcomes of 161 patients undergoing re-do minimally invasive valve operations via mini-thoracotomy (61 patients had aortic) versus 227 patients having CAVR via median sternotomy (177 patients). The authors found a significantly lower early mortality, no wound infection, less need for transfusion and shorter hospital stays in the minimally invasive group. However, the incidence of congestive heart failure, renal disease and poor LV function was significantly higher in the sternotomy group. Furthermore, the multivariate analysis showed that renal disease and poor ejection fraction were associated with increased mortality. The 5-year morality was comparable between the two groups. No subgroup analysis for the aortic group was performed.

In a smaller series by Bakir *et al.* (34) of 19 re-do AVR cases done via upper partial sternotomy (63.2 % patients with previous coronary CABG) there were no early deaths, however, 4 patients (21%) required return to theatre for bleeding including one from an injury to a previous patent vein graft. The mean follow-up time was 23.6 months and there were two late deaths one of unknown cause and one non-cardiac.

Tabata *et al.* (35) reported 146 re-do mini AVRs in an elderly population. The majority (93 patients) had previous CABG. The operative mortality was 4.1%, reoperation rates for bleeding was 0.7% and most of the patients required transfusion (83.6%). In this series, there were no CABG graft injuries and the 5-year actuarial survival was 85%. A small series of ten patients with previous CABG undergoing mini-AVR was also reported by Dell'Amore *et al.* (36). There was no in hospital mortality and no injury to the bypass grafts.

Gaeta *et al.* (37) reported outcomes following re-operative mini-AVR on 16 patients with previous patent left internal mammary artery (LIMA) grafts. On this small series there were no early deaths but four late deaths were reported, out of which two were due to cardiac causes. No patient required conversion to full sternotomy or reopening for bleeding and there were no injuries to the LIMA grafts.

Mikus *et al.* (38) in a series of 90 patients who underwent reoperative aortic valve surgery reported comparative results between a minimally invasive approach cohort (38 patients) and a conventional sternotomy cohort (n=52). There were no significant differences between the groups in terms of the profile risk [e.g., EuroSCORE, LV function or body mass index (BMI)]. There was one death in the minimally invasive group. There were no differences in CPB or AoX times between the two groups however the partial sternotomy group had significantly lower ventilation times.

Kaneko *et al.* (39) reported outcomes following 105 octogenarians that underwent redo isolated AVR. Fifty-one patients underwent mini-AVR while 54 patients had CAVR. Both cohorts had similar risk factors. There

Table 2 Re-do mini-AVR

Author, date	Study type and level of evidence	Patient group	Minimal access approach	Previous cardiac surgery	Outcomes	Comments	Author's conclusions
Byrne *et al.*, 2000 (32)	Retrospective. Level III	34 mini-AVRs, 23 (66%) underwent AVR of the native aortic valve and 11 (33%) underwent replacement of a prosthetic valve	Upper re-sternotomy (inverted "T")	21 patients (62%) had previous CABG and 14 (41%) had previous valve surgery	No intraoperative or valve-related complications; no conversion to full re-sternotomy; 2 (5.9%) early deaths: 1 arrhythmia and 1 stroke; no reoperation for bleeding; morbidity: 3 (9%) new onset AF, 3 pacemaker implantations (9%), 2 deep sternal wound infections (6%); median ICU stay: 1 day; median hospital stay: 7 days; at follow-up (100 % complete, median 19 months): 1 (3%) late deep sternal wound infection, 2.32 (6%) late cardiac deaths		Mini-AVR associated with low morbidity and mortality
Sharony *et al.*, 2006 (33)	Retrospective. Level III	161 patients via mini-thoracotomy for valve surgery (aortic =61; mitral =100) compared with 337 patients who had valve surgery via SS (aortic =160; mitral =177)	Right anterior mini re-thoracotomy	Not specified	Hospital mortality was lower for mini-AVR: 5.6% (9/161) versus 11.3% (38/337) (univariate, P=0.04); mean CPB time (P=0.15) and Aox times similar (0.45), no difference in stroke rates (P=1.00); deep wound infection rates wound infections (0% *vs.* 2.4%, P=0.05), less transfusion (p=0.02) and shorter hospital stay (P=0.009) in mini-AVR patients; higher 5-year survival with mini-AVR (92.4%±2% *vs.* 86.0%±2%, respectively, P=0.08)	Incidence of congestive heart failure, renal disease, and non-elective procedures were higher in the SS group; in multivariate analysis (odds ratio: 95% CI, P value): COPD (P=0.001), renal disease (P=0.01), cerebrovascular disease (P=0.04), and ejection faction <30% (P=0.06) associated with increased mortality	Mini-AVR yields less hospital morbidity, decreased hospital length of stay, and slightly favourable mid-term survival
Bakir *et al.*, 2007 (34)	Retrospective. Level III	19 consecutive patients who had mini-AVR	J-sternotomy	CABG: 12 patients (63.2%) and aortic valve surgery, 6 patients (31.5%)	Mean CPB: 133.1±54.4 and mean AoX: 87.4±32.7; mean intubation time was 1.5±1.4 days, mean ICU stay: 2.9±2.6; mean hospital stays: 12.9±5.7 days, median chest drain output: 550 mL, 4 revisions for bleeding; 2 hospital deaths (5%), 1 sternal wound infection, 3 patients had new-onset AF	Single arm study	Re-do mini-AVR feasible procedure with avoidance of injury to previous coronary grafts

Table 2 (*continued*)

Table 2 (*continued*)

Author, date	Study type and level of evidence	Patient group	Minimal access approach	Previous cardiac surgery	Outcomes	Comments	Author's conclusions
Tabata *et al.*, 2008 (35)	Retrospective. Level III	146 patients, minimally invasive aortic valve surgery	Upper re-sternotomy	109 patients CABG (patent internal thoracic artery graft in 93 patients, 63.7%), previous AVR: 33 (22.6%)	Median CPB: 150 min; mean AoX: 80 min; 4 patients: conversion to full sternotomy; operative mortality was 4.1% (6/146); reoperation for bleeding: 0.7% (1/146); blood transfusion: 83.6% (122/146), no coronary graft injuries; median hospital stay: 8 days; 56% (79/140) patients discharged home, 5-year actuarial survival was 85%	More than 1 previous operation in 13 (8.9%); 19 patients (13%) underwent concomitant procedures: CABG, mitral valve repair or ascending aorta replacement	Re-do mini-AVR feasible and safe procedure with avoidance of injury to previous coronary grafts
Dell'Amore *et al.*, 2009 (36)	Retrospective. Level IV	10 mini-AVR patients	Upper j-shaped mini re-sternotomy	All patients had previous CABG with all grafts patent	No in-hospital mortality, no conversions to full re-sternotomy, no damage to previous grafts, no perioperative MI, 1 patient required pacemaker insertion		Mini-AVR in patients with previous coronary bypass grafting can be performed safely and decreased risk of injury to coronary grafts
Gaeta *et al.*, 2010 (37)	Retrospective. Level III	16 patients that had mini-AVR	J mini-re-sternotomy in 15 patients and inversed "T" mini-re-sternotomy in 1 patient	16 patients with previous CABG and patent LIMA to LAD graft	Mean CPB time was 119.7±38.1 (range: 50–235) min; Mean AoX time was 72±20 (range: 45–125) min; no damage to LIMA; no intra- or perioperative MI, no conversions to full re-sternotomy; no reoperations for bleeding; blood transfusion required in 7 patients; mean ICU stay: 1.6±1.1 days; mean postoperative hospital stay was 7.5±2.6 days; follow-up was 100% complete in (median 58, range 11–124 months): 4 late deaths (2 cardiac related); no prosthesis-related morbidity; survival at 1, 5, and 10 years is 91.6%, 83.3% and 75%, respectively		Mini-AVR feasible in patients with previous patent LIMA to LAD graft

Table 2 (*continued*)

Table 2 (*continued*)

Author, date	Study type and level of evidence	Patient group	Minimal access approach	Previous cardiac surgery	Outcomes	Comments	Author's conclusions
Mikus *et al.*, 2013 (38)	Retrospective. Level III	90 patients who underwent reoperative AVR: 38 mini-aVR and 52 SS	Upper J-shaped mini re-sternotomy	46 had patent bypass grafts and 44 previously had heart valve replacement or repair	Median (IQR) CPB and AoX for mini AVR group were: 67 [28] and 51 [28] min respectively *vs.* 72 [47] and 53.5 [28] min for SS (P=0.686 and P=0.993); ventilation time was less with mini-AVR (P=0.027). Mortality for mini-AVR: 1 (2.6%) *vs.* 3 (5.8%), P=0.476	16 patients had endocarditis as the etiology, and 14 had prosthetic valve endocarditis	Mini-AVR at least as safe as the standard procedure in terms of hospital morbidity and mortality rates
Kaneko *et al.*, 2014 (39)	Retrospective. Level III	105 patients, aged >80 years, isolated valve surgery only: 51 mini-AVR and 54 SS	Upper hemi re-sternotomy		6 patients (5.7%) had reoperation for bleeding, 4 (3.8%) permanent stroke, 4 (3.8%) new renal failure, 22 (21.0%) new-onset atrial fibrillation; operative mortality was 9.2% in the SS group and 3.9% in the mini-AVR group (P=0.438); survival benefit at both 1 year (79%±11.7% *vs.* 92%±7.8%) and 5 years (38%±17.6% *vs.* 65%±15.7%, P=0.028).	No differences in the preoperative risk profiles of the two cohorts; regression analysis identified heparin-induced thrombocytopenia, reoperation for bleeding, older age, full sternotomy, and an infectious complication as predictors of mortality	Acceptable in-hospital outcomes and operative mortality for re-do mini-AVR in high risk cases; survival benefit in mini-AVR patients
Gosev *et al.*, 2015 (40)	Retrospective. Level III	101 patients, isolated valve surgery: 34 mini AVR and 67 SS	Upper hemi-sternotomy	All patients had previous AVR: 57 were bioprosthesis and 44 mechanical	Shorter operative for mini-AVR *vs.* SS: 330 *vs.* 356 min, P=0.053; mini-AVR patients had shorter ventilation time (5.7 *vs.* 8.4 h; P=0.005), ICU stay (37 *vs.* 63 h; P≤0.001) and hospital length of stay (6.5 *vs.* 8.0 days; P=0.038); operative mortality: 1 SS and 0 mini-AVR; survival at 1 and 5 years for mini-AVR versus SS: 100% (95% CI, 100100) and 100% (95% CI, 100100) *vs.* 93.9% (95% CI, 88.299.7) and 85.0% (95% CI, 75.194.9), respectively (P=0.041)		Mini-AVR offers shorter hospital stay, improved mid and long term survival compared to conventional approach

Table 2 (*continued*)

Table 2 *(continued)*

Author, date	Study type and level of evidence	Patient group	Minimal access approach	Previous cardiac surgery	Outcomes	Comments	Author's conclusions
Phan *et al.*, 2014 (13)	Meta-analysis, level II	441 mini-AVR patients from 11 studies	Various: upper mini-sternotomy, "J" mini-sternotomy, mini-thoracotomy, upper mini-sternotomy ("T" and L)	In-hospital mortality	In-hospital mortality 0–9.5%, no difference mini-AVR vs. SS (RR, 0.77; 95% CI, 0.39–1.54; P=0.46); similar stroke rates: 2.6%–8%; no difference in rates of pacemaker implantation, renal failure and reoperation for bleeding; similar CPB durations and AoX times; no difference in hospital stays	Meta-analysis of observational studies (4 single arm and 7 comparative)	Mini-AVR similar efficacy and mortality outcomes compared to SS

Abbreviations: MI, myocardial infarction; RR, risk ratio.

was no difference in terms of operative mortality or other postoperative outcomes between the two approaches, however, the survival analysis at 1 and 5 years favoured mini-AVR.

Gosev *et al.* (40) compared the postoperative outcomes of 34 patients undergoing mini-AVR with 67 patients undergoing CAVR. Both groups did not differ in terms of demographics or preoperative risk profiles. The authors reported shorter operative times, ventilation times, ICU stays and hospital length of stays favouring the mini-AVR group. There was one early death in the CAVR group. Mid-term survival at 1 and 5 years favoured mini-AVR.

In a meta-analysis of seven observational studies of reoperative mini-AVR, Phan *et al.* (41) found similar in-hospital mortality and stroke rates. The rates of PPM implantation, renal failure and re-operation for bleeding were again similar. There was no difference in hospital stays between the two approaches.

Outcomes of mini AVR in patients with high cardiac risk scores

In the current section we will discuss the studies that reported outcomes of mini-AVR in populations considered high risk according to the various risk scoring systems in cardiac surgery (*Table 3*).

Bridgewater *et al.* (42) reported outcomes of a high risk cohort (median age 78 and Parsonnet score of 18%) who underwent mini-AVR via a transverse sternotomy approach compared to a Parsonnet score, age and sex matched retrospective cohort. The authors found a significantly higher mortality, incidence of re-exploration, paravalvular leaks and re-exploration in mini-AVR group. Furthermore, mini-AVR had longer postoperative stays and higher incidence of morbidity.

In 2004, De Smet *et al.* (43) analysed the outcomes of 100 patients undergoing mini-AVR via J-sternotomy compared to a retrospective series of CAVR performed in 91 patients operated before introduction of mini-AVR in that institution. Both cohorts had similar preoperative characteristics and they were further stratified by EuroSCORE in low, medium and high risk. In the high risk group (EuroSCORE >6) there was a higher incidence of AF in patients undergoing sternotomy in contrast to mini-AVR patients who experienced more neurologic events. However, when only the severe brain injuries were included in the analysis no difference was noted. Similarly, a greater incidence of AF occurred in the medium risk sternotomy group. In the low risk mini-AVR patients, there was a higher incidence of AF. Overall, the mortality

Table 3 Mini-AVR in patients with high cardiac surgery risk score

Author, date	Study type and level of evidence	Patient group	Cardiac risk score	Minimal access approach	Outcomes	Comment	Conclusions
Bridgewater *et al.*, 1998 (42)	Retrospective, level IV	14 patients (median age 78) mini-AVR patients compared with a historical CAVR group (n=14)	Mean Parsonnet score of 18%	Transverse sternotomy	AoX and CPB times (67 and 92 min for mini-AVR versus 46 and 66 min respectively for SS AVR, P=0.001); hospital stay; median 12 days for mini-AVR *vs.* 8 days for SS AVR, P=0.025; 2 *vs.* 0 deaths (P=0.16) in the mini-AVR group, in the mini-AVR group: 2 re-explorations for bleeding, 3 new paravalvular leaks compared to none in the control group (P=0.07), 1 patient had CVA and 1 patient had respiratory failure; in the control group there was 1 patient with new onset of renal failure and 1 wound dehiscence	Patients matched for surgeon, age, sex and Parsonnett score	A greater level of morbidity and mortality is associated with mini-AVR
De Smet *et al.*, 2004 (43)	Retrospective study, level III	100 patients mini-AVR and 99 patients SS AVR	Patient stratified into low, medium and high risk groups according to EuroSCORE; high risk patients: 51 mini-AVR *vs.* 40 SS AVR	J-shaped mini-sternotomy	In the high risk group: more CAVR patients had new onset AF: 15 (29.4%) *vs.* 21 (52.5%), P=0.001 while more neurological events occurred in the mini-AVR group: 3 (5.8%) *vs.* 1 (2.5%), P=0.001; no differences in terms of mortality, sternal or other infection	Overall no differences in: AoX time, CPB time, ICU blood loss, ICU and hospital stays	In high risk patients using a minimally invasive approach proves beneficial in terms of cardiac rhythm disturbance
Grossi *et al.*, 2008 (44)	Retrospective study, level III	731 patients with EuroSCORE of 7 or higher undergoing isolated mini-AVR	Mean EuroSCORE was 9.7 (median, 10), and the mean logistic EuroSCORE was 17.2%	Right anterior mini thoracotomy in 436 (92.9%), upper mini-sternotomy approach in 33 (7.1%)	Actual hospital mortality was 7.8% (57 of 731); in multivariate analysis: ejection fraction of <30% (P=0.002; OR, 3.13), chronic obstructive pulmonary disease (P=0.019; OR, 2.14), and peripheral vascular disease (P=0.048; OR, 2.13) were predictors of hospital mortality; freedom from all-cause death (including hospital mortality) was 72.4% at 5 years (152 patients); age (P<0.001), previous cardiac operations (P<0.014; OR, 1.51), renal failure (P<0.002; OR, 2.37), and chronic obstructive pulmonary disease (P<0.007; OR, 1.30) were predictors of worse survival	Single arm design	Logistic EuroSCORE greatly over predicts mortality in these patients that could benefit from mini-AVR rather than TAVI

Table 3 (*continued*)

Table 3 (*continued*)

Author, date	Study type and level of evidence	Patient group	Cardiac risk score	Minimal access approach	Outcomes	Comment	Conclusions
Martens *et al.*, 2009 (45)	Retrospective, level IV	22 patients, age >79, sutureless mini-AVR using sutureless ATS 3f Enable aortic bioprosthesis	Mean logistic EuroSCORE was 13	Partial upper sternotomy	Valve implantation time:10±6 min; CPB time:87±16 min; AoX: 55±11 min; early mortality (90 days): 9% (2 patients); no paravalvular leaks, mean transvalvular gradients: at discharge and 9±6, 8±2 mmHg at 1 year	Concomitant subvalvular myectomy in 2 patients	Sutureless mini-AVR in elderly, high risk elderly patients is feasible, safe and results in good in early and mid-term haemodynamic performance
Concistre *et al.*, 2013 (46)	Retrospective, level IV	13 patients, mean age 77±3.9 years, sutureless mini-AVR, ATS 3f Enable aortic bioprosthesis	Mean, SD logistic EuroSCORE was 15%±3.5%	V-type mini-sternotomy interrupted at the second intercostal space	Mean CPB time: 100.2±5.3 min; AoX: 66.4±18.6 min, no hospital mortality, short term mean ± SD pressure gradient: 14±4.9 mmHg [median follow-up time was 4 months (IQR, 2–10 months)]		Sutureless mini-AVR in high risk elderly patients is feasible, safe and with good haemodynamic results
Burdett *et al.*, 2014 (47)	Retrospective, level III	98 patients mini-AVR and 93 patients CAVR	Mean logistic EuroSCORE mini-AVR 7.15 *vs.* SS AVR 6.55, P=0.47)	Manubrium-limited sternotomy	Mean CPB time (mini-AVR *vs.* SS AVR): 88 *vs.* 78 min, P=0.00040; mean AoX (mini-AVR *vs.* SS AVR): 66 *vs.* 60 min, P=0.0078, less postoperative blood loss (332 *vs.* 513 mL, P=0.00021); mini-AVR less likely to require blood products (24% *vs.* 36%, P=0.042), no difference in: length of stays, survival, need for dialysis for AKI, stroke, AF rates, PPM rates or deep sternal wound infection		Mini-AVR confers similar outcomes to CAVR; additional benefits with mini-AVR in reducing blood loss and need for transfusion

and lengths of stay were similar between conventional sternotomy versus mini-sternotomy.

Grossi *et al.* (44) reported outcomes of isolated AVR in a high risk cohort of 731 patients with mean EuroSCORE of 9.7. Mini-AVR was performed in 64.2% (469 patients). No comparative analysis was performed between the operative approaches. The actual hospital mortality was 7.8% suggesting that the EuroSCORE over predicted the mortality. In the multivariate analysis; poor ejection fraction, chronic obstructive pulmonary disease (COPD) and peripheral vascular disease significantly affected hospital mortality. The 5-year freedom from all-cause mortality was 72.4% at 5 years. Age, reoperation, renal and chronic lung disease were predictors of worse survival.

Martens *et al.* (45) reported outcomes of mini-AVR via partial sternotomy, using the ATS 3f Enable sutureless bioprosthesis, in 22 elderly patients. Mean age of 75 years and mean logistic EuroSCORE of 13. The mean reimplantation time was 10±6 min, CPB time was 87 min and the mean cross clamp time was 55 min. The early mortality (<90 days) was 9% (2 deaths). There were no paravalvular leaks and the implanted valves had low gradients both on discharge and at 12 months.

Later, in 2013, Concistre *et al.* (46) reported outcomes in an elderly population (mean age of 77) undergoing sutureless aortic valve implantation (3f Enable bioprosthesis) via V-type mini-sternotomy. The mean EuroSCORE of the cohort was 15%. The mean CPB and aortic cross clamp times were 100.2 and 66.4 min respectively. One patient had trivial paravalvular leak and there were no early deaths or at follow-up (median follow-up time was 4 months, interquartile range, 2–10 months). The mean pressure gradients were remained low on follow-up. Burdett *et al.* (47) compared two matched cohorts for perioperative profile and risk score (mean EuroSCORE of 7). One group (98 patients) underwent manubrium limited sternotomy and the other conventional sternotomy (93 patients). The mini-AVR cohort had longer CPB times and aortic cross clamp times (10 and 6 min respectively) but significantly less postoperative blood loss and transfusion requirements. The postoperative morbidity, length of stays, rate of paravalvular leaks and in hospital mortality were similar.

Mini AVR in patients with chronic lung disease or pulmonary hypertension

As discussed earlier, maintenance of the sternal integrity could prove beneficial in patients with reduced respiratory reserve. Calderon *et al.* (48) in a prospective randomized trial of mini-AVR versus CAVR measured the postoperative spirometry parameters in 78 patients. They found no significant changes between the two groups.

Stolinski *et al.* (49) measured the pulmonary function tests at 1 week, 1 month and 3 months of two elderly cohorts (mean age >75 years): mini-AVR (65 patients) versus CAVR (82 patients). The two cohorts had similar perioperative characteristics. At 1 week and 1 month the pulmonary function was better in the mini-AVR but there was no significant difference between the two groups at 3 months. The duration of postoperative mechanical ventilation was lower in the mini-AVR group but the incidence of pulmonary complications was similar.

A study by Li *et al.* (50) measured the extravascular water index and pulmonary vascular permeability index in 90 patients that received either a conventional sternotomy, mini-AVR via right anterior thoracotomy or via upper sternotomy. The minimally invasive groups had a faster recovery of the above parameters.

Only a few studies evaluating the effect of mini-AVR in patients with poor lung function pre-operatively exist. Albacker *et al.* (51) in a propensity matched study of 223 patient pairs: mini-AVR via J-sternotomy versus AVR via full sternotomy found a shorter ICU and hospital length of stay for mini-AVR patients as the forced expiratory volume in 1 second (FEV1) decreased. There was a trend towards higher survival of mini-AVR patients (93% versus 89% at 1 year, P=0.07) however there was no difference in late survival.

A retrospective analysis of 165 patients with COPD (82% had moderate COPD, e.g., FEV1 between 50% and 80%) by Santana *et al.* (52) found no difference in hospital mortality between the mini-AVR patients (n=100) and the conventional sternotomy patients (n=65). However, the composite of post-operative complications was significantly reduced in mini-AVR groups. Furthermore, the ICU lengths of stay and hospital length of stay were shorter in minimally invasive group.

Gosain *et al.* (53) reported outcomes after mini-AVR in 569 patients with pulmonary hypertension. The mean pulmonary artery pressure of the group was 33 mmHg. The overall early mortality was 3.5% and the stroke rates were 1.4%. Patients with severe pulmonary hypertension had a significantly longer ICU stay and trend towards longer ventilation times.

Mini AVR in patients with renal dysfunction

Pre-operative renal dysfunction is an independent risk factor in operative mortality and late survival in patients undergoing heart surgery (54). The renoprotective effect of minimally invasive surgery has already been proven in mitral valve surgery (55,56).

We found only two studies that evaluated the effect mini-AVR in patients with pre-existing renal dysfunction. Valdez *et al.* (57) retrospectively reviewed a cohort of 688 patients with chronic kidney disease stages 2–5. In their study, 236 patients received a mini-AVR and 87 received a CAVR. There were no differences in operative mortality between the two groups. The mini-AVR group had a lower incidence of acute on chronic kidney injury despite longer CPB and AoX times. However, there was no difference in the peak postoperative creatinine measurements between the two groups or the need for dialysis. The authors used the RIFLE (risk, injury, failure, loss of kidney function, and end-stage kidney disease) classification to define acute kidney injury (AKI). This classification also takes into account urine output and the estimated glomerular filtration rate. Furthermore, the mini-AVR patients had fewer composite complications, shorter ICU and hospital lengths of stay. In the multivariate analysis minimally invasive surgery was associated with 60% reduction in the risk of development of AKI. Similar results were found by a large meta-analysis of non-randomized controlled trials where renal failure occurred less in the mini-AVR group despite longer CPB and AoX times (13).

Haldenwang *et al.* (58), in a small retrospective study compared 77 patients that received a mini-AVR to 56 patients that received a TAVI. The mini AVR patients had a lower risk of developing AKI compared to TAVI.

Patients with poor LV function or severe heart failure

The study by Tabata *et al.* (59) is the only one to date that compares the effect of mini-AVR versus CAVR in patients with pre-operative LV dysfunction. The authors propensity matched two cohorts of 41 patients each (mini-AVR or CAVR). There was no significant difference in operative mortality, post-operative complications, blood transfusion requirement or length of hospital stay and CPB and AoX times.

A study conducted by Mihaljevic *et al.* (60) compared two propensity matched cohorts of patients with severe heart failure (New York Heart Association III and IV): minimally invasive valve surgery versus conventional sternotomy valve surgery. The mean ejection fraction did not differ between the groups and was classed as moderate. The comparisons were adjusted not only to the patient characteristics but also to the individual surgeon. Without adjusting for the operator, the CPB, aortic cross clamp times and ICU length stays were shorter for the minimally invasive group. The hospital mortality, long-term survival were similar. However, when adjusting for the surgeon there were no differences in the outcomes between the two groups.

Mini AVR in obese patients

Several studies found no adverse outcomes of performing conventional cardiac surgery in obese patients. However, this group of patients is at increased risk of deep sternal wound infection, therefore a minimally invasive approach could prove advantageous (61,62). In contrast, adequate exposure using a minimally invasive approach can prove to be a challenge. Two studies to our knowledge evaluated the effect of mini-AVR in this high-risk group (*Table 4*). Santana *et al.* (62) compared the outcomes of 31 patients who had mini-AVR via a mini-thoracotomy with a matched group 43 patients had CAVR. The composite of postoperative complications occurred less frequently in the minimally invasive group. This was driven by a lower incidence of renal failure, shorter ventilation times, lower reintubation rates, lower incidence of deep sternal wound infection and reduced in-hospital mortality. A recent study by Acharya *et al.* (63) on 90 patients who underwent mini-AVR compared using univariate regression analysis on the effect on postoperative outcomes of a BMI <25 (in 36 patients) with the effect of BMI ≥25 (54 patients). The high BMI cohort had increased incidence of hospital acquired pneumonia and new onset of AF. However, there was no difference in ICU length of stay, hospital length of stay, wound complications rates, inotrope requirements or renal dysfunction. Furthermore, a correlation between increasing BMI and reduced ventilation or post-operative blood loss was found.

Mini-AVR in patients requiring concomitant procedures

Another high-risk group is that of patients requiring additional, complex procedures associated to minimally aortic valve surgery.

Totaro *et al.* (64) reported the outcomes of 1,126 procedures

Table 4 Mini-AVR in patients with poor lung function, pulmonary HTN, poor LV, renal failure and in patient requiring concomitant procedures.

High risk group	Author, date and journal	Study type and level of evidence	Patient group	Minimal access approach	Outcomes	Comments	Conclusion
Poor lung function	Albacker *et al.*, 2014 (51)	Retrospective, propensity matched, level III	223 propensity-matched pairs of patients with measured FEV1%: mini-AVR versus CAVR identified from 6,931 consecutive isolated AVRs	Partial upper J-incision	Patients with chronic lung disease had a longer median ICU stay (41 *vs.* 27 h, P=0.001) and postoperative length of stay (7.1 *vs.* 6.1 days, P<0.0001); at normal values of FEV1% no difference between mini-AVR and CAVR however at progressively lower FEV1% length of stays were shorter with mini-AVR; trend toward better survival with mini-AVR (93% *vs.* 89% at 1 year, P=0.07) but survival at 5 years was no longer different (P=0.9), greatest survival advantage persisting at 5 years in patients with FEV1% <50		Patients with poor pulmonary function pre-operatively would benefit from mini-AVR in terms of ITU length of stay and overall length of hospital stay; better survival with mini-AVR as lung function decreases
	Santana *et al.*, 2012 (52)	Retrospective, level III	165 patients undergoing isolated valve surgery who had diagnosed COPD. 100 patients mini-AVR *vs.* 65 patients SS AVR	Mini-sternotomy	Of the 165 patients with diagnosed COPD, in hospital mortality (mini-AVR *vs.* CAVR): 1% *vs.* 5%, P=0.14; composite of postoperative complications reduced in mini-AVR (30% versus 54%, P=0.002); median ICU stay (mini-AVR *vs.* CAVR): 47 h (IQR 40–70 h) versus 73 h (IQR 51–112 h), P<0.001; median postoperative length of stay (mini-AVR *vs.* SS AVR): days (IQR 5–9 days) versus 9 days (IQR 7–13 days), P<0.001; median CPB time (mini-AVR *vs.* CAVR): 118 (102–140) *vs.* 80 (60–106) min, P<0.001; AoX (mini-AVR *vs.* CAVR): 84 (71–102) *vs.* 53 (41–74) P<0.001, more transfusion of red blood cells with CAVR (P<0.001)	Composite of postoperative complications included: death, renal failure, prolonged ventilation, re-intubation, sternal deep wound infection, sepsis, pneumonia, bleeding requiring re-operation, stroke, atrial fibrillation	In patients with diagnosed COPD a minimally invasive approach is beneficial in terms of length of hospital stay and reduced post-operative complications

Table 4 (*continued*)

Table 4 (*continued*)

High risk group	Author, date and journal	Study type and level of evidence	Patient group	Minimal access approach	Outcomes	Comments	Conclusion
Pulmonary HTN	Gosain *et al.*, 2016 (53)	Retrospective, level III	569 patients (mean age 72±11) following minimally invasive aortic/mitral valve replacement with mild to severe pulmonary HTN	Right mini-thoracotomy	Mild/moderate pulmonary HTN (n=474) *vs.* severe pulmonary HTH (n=95): no difference in operative mortality, postoperative stroke rates; need for intraoperative transfusion or ventilation times; ICU length of stay shorter for mini-AVR (46±10 *vs.* 70±12, P<0.001) bur no difference in hospital length of stay (P=1)	Mean pulmonary artery pressure (mPAP) was classed as mild (mPAP 25–29 mmHg), moderate (30–39 mmHg), severe (mPAP >39 mmHg)	Mini-AVR safe and feasible in patients with PH
Renal dysfunction	Valdez *et al.*, 2013 (57)	Retrospective, level III	688 patients with chronic kidney stages 2 to 5 who underwent either minimally invasive valve surgery (510, 74%), or conventional valve surgery (178, 26%)	Right mini-thoracotomy for mini-AVR and left mini-thoracotomy for mitral valve surgery	Less composite complication with mini-AVR: (33.1% *vs.* 49.4%; OR, 0.5; P≤0.001); shorter intensive care unit [48 (IQR, 33–74) *vs.* 71 (IQR, 42–96) h; P<0.01]; hospital stay [8 (IQR, 6–9) days *vs.* 10 (IQR, 8–15) days; P<0.001); lower incidence of acute kidney injury (8% *vs.* 14.7%; OR, 0.5; P≤0.01); in multivariable analysis, minimally invasive valve surgery associated with a 60% reduction in the risk of postoperative acute kidney injury	Composite of complications included: AF, pneumonia, reintubation, stroke, sepsis, wound infection, prolonged ventilation, bleeding requiring reoperation +F5:G5	Minimally invasive valve surgery for patients with pre-existing CKD stages 2–5 associated with reduced postoperative complications and risk of acute on chronic renal failure
	Haldenwang *et al.*, 2014 (58)	Retrospective, level III	70 patients, age >75 years, undergoing TAVI *vs.* 56 mini-AVR	J-shape sternotomy	58 patients developed a risk of AKI (creatinine >0.3 mg/dL or 1.5–1.9-fold creatinine increase from baseline) and 13 had renal injury or failure (>2-fold creatinine increase from baseline): higher AKI risk for TAVI (OR =2.58; 95% CI, 1.18–5.63; P=0.017), no correlation between AKI and early mortality	EuroSCORE II and preoperative creatinine higher for TAVI *vs.* mini-AVR (P<0.01), eGFR higher in in mini-AVR patients (P=0.01) but these parameters had no impact on AKI on further analysis (logistic regression)	A higher risk for AKI after TAVI should be considered in elderly patients

Table 4 (*continued*)

Table 4 (*continued*)

High risk group	Author, date and journal	Study type and level of evidence	Patient group	Minimal access approach	Outcomes	Comments	Conclusion
Poor LV	Tabata *et al.*, 2007 (59)	Retrospective, propensity matched, level III	140 patients with ejection fraction ≤40% undergoing isolated AVR: 73 patients mini-AVR and 67 CAVR	Upper hemi-sternotomy	Operative mortality was comparable between mini-AVR and CAVR (2.4% *vs.* 4.8%, P=0.562); no difference in: CPB time, AoX times, reoperation for bleeding, blood transfusion requirement, ventilation times, perioperative MI, renal failure, cerebrovascular events, deep sternal wound infection or length of hospital stay, or discharge to home rates		Mini-AVR in patients with poor left ventricular function can be performed safely with comparable results to CAVR
	Mihaljevic *et al.*, 2014 (60)	Retrospective, propensity matched, level III	Matched pairs of patients with NYHA class III–IV who underwent minimally invasive valve surgery (n=185) *vs.* 185 pairs conventional surgery; further adjustment for surgeons: 139 minimally invasive valve surgery *vs.* 138 conventional surgery	Upper hemi-sternotomy	Minimally invasive surgery versus conventional sternotomy provided shorter AoX time (59±27 *vs.* 64±26 min), CPB time (75±35 *vs.* 86±34 min), ICU stays (24 *vs.* 43 h, P=0.007); hospital morbidity, mortality, long-term survival were similar; after adjusting for surgeon: all outcomes were similar, including AoX times, CPB times, ICU, hospital stays and survival	Mixed aortic and mitral surgery	In patients with poor LV a minimally invasive approach provides comparable post-operative results when compared to median sternotomy approach
Obese patient	Santana *et al.*, 2011 (62)	Retrospective, level III	160 obese patients with (BMI of greater than 30 kg/m^2) undergoing isolated valve surgery: 64 underwent minimally invasive isolated valve surgery compared to 96 via conventional surgery	Right minithoracotomy	Composite postoperative complications: 15 (23.49%) versus 49 (51.0%), P=0.034, in the minimally invasive group versus median sternotomy; minimally invasive valve surgery associated with: lower incidence of acute renal failure (0 *vs.* 6 patients (6.25%), P=0.041), shorter ventilation times: prolonged intubation [12 (18.7%) *vs.* 33 (34.3%), P=0.049]; lower reintubation rates [3 (4.68%) *vs.* 15 (15.6%), P=0.032], less deep sternal wound infections: [0 *vs.* 4 (4.1%), P=0.098], and death [0 *vs.* 8 (8.3%), P=0.041]	Mixed aortic and mitral surgery	Minimally invasive surgery in obese patients has a lower morbidity and mortality when compared with conventional surgery

Table 4 (*continued*)

Table 4 (*continued*)

High risk group	Author, date and journal	Study type and level of evidence	Patient group	Minimal access approach	Outcomes	Comments	Conclusion
	Acharya *et al.*, 2016 (63)	Retrospective, level III	90 patients receiving mini-AVR. Univariate linear regression analysis performed to examine the effects of BMI (≥25 *vs.* <25) on post-operative outcomes	J-shaped sternotomy	Overall no peri-operative mortality, myocardial infarction or stroke; patients with BMI ≥25 had: longer AoX times (P=0.0218), trend towards longer CPB times (P=0.0615), higher incidence of hospital acquired pneumonia (P=0.020) and new onset of AF (P=0.036); no effect of raised BMI on ICU and hospital stays; similar rates between groups of infection, inotrope requirements and renal dysfunction; increasing BMI correlated with reduced mechanical ventilation (P=0.039) and blood loss (P=0.004)	Single arm study design	Mini-AVR can reduce obesity related complications
Concomitant procedure	Totaro *et al.*, 2009 (64)	Retrospective, level III	1,126 procedures minimally invasive aortic procedures: 695 patients undergoing isolated aortic valve surgery (61%) *vs.* 77 patients who had re-do mini-AVR *vs.* complex procedures performed in 354 (32%)	Upper mini-sternotomy	Overall in-hospital mortality was 4.1%; complex minimally invasive surgery associated with significantly higher postoperative mortality (24 patients, 6.7%) than isolated procedures or re-do mini-AVR; ventilation times (P<0.05), ICU stays (P<0.05) and bleeding (P<0.05) higher for complex group *vs.* isolated or re-do groups; hospital stay longer for complex groups *vs.* isolated AVR (P<0.05, no differences in conversion to full sternotomy or surgical revision across the three groups	Complex procedures included: double valve replacement-repair, ascending aorta-aortic arch replacement, aortic root replacement, aortic dissection, AVR combined with coronary surgery, and complex redo procedures	Minimally invasive approach for complex procedures safe and feasible

Table 4 (*continued*)

Table 4 (*continued*)

High risk group	Author, date and journal	Study type and level of evidence	Patient group	Minimal access approach	Outcomes	Comments	Conclusion
	Kaneko *et al.*, 2012 (65)	Retrospective, level III	109 patients undergoing mini-AVR combined with aortic surgery	Upper hemi-sternotomy	Operative mortality was 2.8% (n=3); 4 (3.7%) reoperations for bleeding; mean CPB time: 152±61 min; AoX time: 108±47 min; 2 (1.8%) myocardial infarctions, 2 (1.8%) new-onset renal failure; mean length of stay was 7.1±5.6 days; 1-year survival was 96.2% and 5-year survival was 92.4%	Single arm study design; associated aortic procedures included: supra coronary ascending aortic replacement (n=65), ascending and proximal arch replacement, (n=8 patients), aortoplasty (n=11 patients), Bentall procedure (n=8), root enlargement (n=13)	Mini-AVR combined with aortic surgery is safe and feasible and associated with good early outcomes
	Elmahdy *et al.*, 2010) (66)	Retrospective, level IV	6 patients undergoing minimally invasive triple valve surgery patients: 5 mini-AVR and 1 minimally invasive aortic valve repair combined with tricuspid valve repair and mitral valve repair	Right anterior thoracotomy approach	2 early deaths; 2 patients had new onset of AF; no postoperative cerebrovascular accidents, myocardial infarctions or acute kidney injuries; median ICU stay: 62 h (IQR: 50–111 h); median hospital stay: 12 days (IQR: 7–23 days)		Minimally invasive triple valve surgery safe and feasible

Abbreviations: FEV1, forced expiratory volume in 1 second; TAVI, transcatheter aortic valve insertion; eGFR, estimated glomerular filtration rate; mPAP, mean pulmonary artery pressure.

performed via upper mini-sternotomy. The authors compared the outcomes of isolated mini-AVR (61%) with re-do mini-AVR (7%) or other complex cardiac surgery (32%) including AVR combined with aortic surgery procedures or CABG. The complex cardiac surgery group had a higher operative mortality, longer ventilation times and longer ICU status however the surgical revision rates were similar in all three groups.

Kaneko *et al.* (65) reported outcomes of mini-AVR via an upper hemi-sternotomy in 119 patients who required a concomitant aortic procedure. The majority of the patients (59.6%) had supra-coronary ascending aorta replacement. The authors reported an operative mortality of 2.8% and a postoperative survival at 1 and 5 years of 96.2% and 92.4% respectively. There were 4 (3.7%) reoperations for bleeding. Other complications included postoperative renal failure in two cases and myocardial infarction in two other cases. The mean length of stay was approximately a week.

Elmahdy *et al.* (66) reported a case series of six patients that had triple valve surgery via a right anterior mini-thoracotomy. All patients had aortic valve surgery, mitral valve repair and tricuspid valve repair. The authors reported two early deaths and two cases of postoperative AF.

Sutureless mini-AVR in high risk patients

Rapid deployment valves (RDV) or sutureless valves had been developed with excellent perioperative outcomes and are increasingly used (67-70). Currently, RDV-AVR can be performed using either the self-expanding Perceval S (LivaNova Group, Milan, Italy) or the rapid-deployment Intuity Elite (Edward Lifesciences, Irvine, USA) (71). Some authors showed that the AoX and CPB times are independent predictors of mortality and morbidity after cardiac surgery (72). Hence, the reduced time taken to deploy these valves could potentially translate into better outcomes, especially in the high-risk patients. Phan *et al.* in a meta-analysis of observational studies found RDV-AVR to be safe and associated with shorter AoX and CPB duration and with comparable complication rates to the conventional approach in the short-term (70). Furthermore, the ease of placement of these valves makes them suitable to be inserted using a minimally invasive approach (70,71). Therefore, minimally invasive RDV-AVR could prove to be a significant competitor of TAVI, particularly in the high risk patients. In a recent multicenter propensity matched study comparing outcomes of 214 patients matched to either RDV-AVR or TAVI, there was no difference in 30-day or 1-year mortality, stroke, bleeding or myocardial infarction (73). However, the RDV-AVR patients had a higher procedural success rate and less incidence of paravalvular leaks at the cost of higher incidence of pacemaker insertion compared to the TAVI cohort. Conversely, the TAVI cohort had a significantly shorter ICU stay and hospitalization duration and significantly lower peak and mean aortic gradients. The main advantage of RDV-AVR is the resection of the native valve and the annular decalcification that could translate into better haemodynamic profiles and possibly better long-term outcomes, which would be pertinent in younger patients (71). Similarly to TAVI literature, there is a paucity of long-term follow-up studies of RDV-AVR. Englberger *et al.* (68) reported excellent haemodynamic profiles, very low re-operation rates and no structural valve deterioration at 5 years, in a cohort of 141 patients undergoing RDV-AVR.

Patients with small aortic root are prone to patient prosthetic mismatch which could result in poorer outcomes (74). In high-risk patients, adding aortic root enlargement with prolongation of surgery may lead to detrimental effects. Hence, the use of RDV may prove to be a better strategy (75). Other groups that can benefit from RDV-AVR are the patients with severe aortic root calcification (76) or re-do AVR (77) where inserting stitches for conventional valves may prove to be very difficult or sometimes virtually impossible. Certainly, well designed randomized trials comparing TAVI with RDV-mini-AVR with long-term follow-up are needed to find out the best alternative in high risk cohorts.

Limitations of the current evidence

The evidence presented in the current review suggests that mini-AVR in the various high risk categories can be performed with comparable survival to conventional techniques but with several additional benefits. However, we have to acknowledge several limitations to the conclusions we draw. Firstly, most of the studies we found were single centre, non-randomized and retrospective. Furthermore, both the patients and medical staff were not blinded to the treatment modality. Efforts were made to balance the groups by propensity matching or cardiac risk score matching in the comparative studies, but this does eliminate patient selection bias entirely. We also found heterogeneity of the available data in terms of the postoperative outcomes. Some studies showed that mini-AVR could reduce various events such as renal failure transfusions etc. in contrast to other studies that did not show this. Very few studies

included other valve surgery that lacked sub-analysis for aortic procedures. In this review, we also looked at series of mini-AVR using sutureless aortic valves. In such cases, the improved outcomes could well be attributed to the sutureless valve rather than the minimally invasive approach. Finally, there was heterogeneity in the type of minimally invasive approach used that could influence the outcomes.

Conclusions

All the current evidence on the performance of mini-AVR in high risk patient groups is based on retrospective, observational studies. In all high-risk groups, mini-AVR is performed with comparable morality and mid-term survival to CAVR. In elderly patients, despite longer AoX and CPB times, mini-AVR results in improved ventilatory function and renal function, reduced wound infection, shorter hospitalization and a greater proportion of patient being discharged straight to home. Re-do mini-AVR is a safe procedure with some studies showing a benefit in mid-term survival. Mini-sternotomy in patients with previous CABG can be performed with a low risk of injury to patent grafts. Current cardiac surgery scoring systems tend to overestimate mortality in high risk patients. Despite longer operative times and longer hospitalization, RDV-mini-AVR is a competitive alternative to TAVI in the high-risk patient. In patients with chronic lung disease, pulmonary hypertension or chronic kidney disease, a minimally invasive approach is safe and reduces hospital and ICU length of stays. Obese patients can benefit from a minimally invasive approach in terms of reduced wound complications, improved respiratory function and improved survival according to a study. Mini-AVR concomitant with aortic surgery or valve surgery can be performed with acceptable mortality and morbidity.

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Footnote

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