Exploring the impact of left ventricular diastolic dysfunction on postoperative cardiac surgery outcomes, with a focus on sex disparities: a comprehensive literature review

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Introduction: Left ventricular diastolic dysfunction (LVDD) is known to cause worse outcomes after cardiac surgery. Females have twice the risk of developing LVDD compared with males. The aim of this literature review was to evaluate the association between LVDD and early (≤30 days) outcomes after cardiac surgery, including sex disparities.

Methods: We identified 454 studies in Medline and Embase, of which 19 were included. Articles were assessed for inclusion of female patients with LVDD, ≥50 years of age undergoing cardiac surgery (on or off-pump) or transcatheter aortic valve replacement. The primary outcome was early postoperative mortality. Secondary outcomes were early postoperative complications, ICU length of stay (ICULOS), hospital length of stay (HLOS), and other sex-related postoperative outcomes.

Results: In patients with LVDD, the majority of studies showed that higher LVDD grades correlate with higher early postoperative mortality. In patients with LVDD, who underwent on-pump cardiac surgery, female sex was significantly associated with higher LVDD grades and baseline E/e' ratios. Females with LVDD, were associated with prolonged HLOS after off-pump coronary artery bypass grafting (CABG). In combined cardiac surgery, a twofold increased risk of prolonged HLOS and increased ICULOS was reported. Furthermore, increased left ventricular end-diastolic filling pressure, an increased need for postoperative inotropic support, and difficult separation from cardiopulmonary bypass were observed.

Discussion: Despite the limited number of studies focusing on sex differences, females with LVDD appear to have worse early outcomes after cardiac surgery compared to men with LVDD. Future research will need to identify sex-specific risk factors and target treatment optimization.

Introduction

Left ventricular diastolic dysfunction (LVDD) is defined as abnormal or restrictive relaxation and filling of the left ventricle (1, 2). This increases left ventricular end-diastolic pressure (LVEDP) and impairs the filling ability of the ventricle (2). Causes of LVDD include coronary artery disease, hypertension, and valvular heart disease (3). LVDD can be classified into three grades of severity based on echocardiographic parameters (Table 1) (2).

Females are twice as likely to develop LVDD as males of the same age (4). Vascular stiffening is a major pathophysiological factor contributing to the higher prevalence of LVDD in females. With aging, ventricular elastance decreases more rapidly in females (5). In addition, comorbidities such as iron deficiency, diabetes mellitus(DM), obesity, hypertension, and pre-eclampsia are associated with the increased incidence of LVDD in females by inducing an inflammatory response (5).

If LVEDP is elevated in patients with LVDD, circumstances such as tachycardia or elevated afterload can lead to an increase in left atrial pressure(LAP), causing pulmonary congestion, which may cause subsequent symptoms such as dyspnea and hypoxia (6, 7). With further deterioration of the disease, heart failure (HF) can occur. If the left ventricle ejection fraction is preserved (LVEF >40%), this form of HF is defined as Heart Failure with Preserved Ejection Fraction (HFpEF). While HF in general affects 1%–2% of the adult population worldwide, it is a growing cause of significant morbidity and mortality (8, 9). HFpEF accounts for 30%–50% of patients with HF, and incidence increases with age (10).

In the perioperative period, surgery, inflammation and stress can induce tachycardia, hypertension, high cardiac output, or volume shift, which can separately or in combination worsen existing LVDD contributing to the development of HFpEF (11).

Several studies of non-operative patients treated conservatively have investigated whether there are sex differences in the outcomes of patients with LVDD (12–17). These studies showed that females

with LVDD had similar outcomes in terms of in-hospital and all-cause mortality compared to males with LVDD. In addition, the incidence of cardiac death and hospitalization due to LVDD was lower in females.

In cardiac surgical patients, the presence of LVDD was associated with higher postoperative mortality and serious adverse cardiac events after surgery such as postoperative atrial fibrillation (POAF) (18). Female patients are more likely to develop LVDD, potentially increasing their risk of mortality and morbidity compared to males. However, there is currently no research into whether female sex exacerbates the adverse effects on postoperative outcomes in LVDD patients (19, 20).

Our intention was therefore to evaluate whether LVDD predicts worse early outcomes (≤30 days) after cardiac surgery, in female patients compared with male patients, with similar baseline characteristics. For this reason, we conducted a literature review to assess the effect of LVDD—by sex—on the early cardiac surgical outcomes (mortality and morbidity) after on- and off-pump cardiac surgery and surgical and percutaneous aortic valve procedures.

Materials and methods

We defined keywords relevant for this review: left ventricular dysfunction, diastolic dysfunction, LVDD, HFpEF, cardiac surgery, echocardiography, females, and postoperative outcomes. These keywords were used to find MeSH (Medical Subject Headings)- and related terms to build the search, which was performed in April 2023. Articles were included if written in English, Dutch, or German and published on Medline or Embase between January 2000 and April 2023. Articles were assessed for further evaluation if they included female patients with LVDD (grade I–III), aged ≥50 years that underwent cardiac surgery (on-pump or off-pump) or transcatheter aortic valve replacement (TAVR). Articles regarding pediatric cardiac surgery, congenital cardiac surgery, case reports, case series, and *in vitro* and animal studies were excluded.

The following data was extracted from the studies: early postoperative mortality (≤30 days) after cardiac surgery, early postoperative complications (≤30 days), ICULOS, HLOS, LVDD grades, E/e' ratios at baseline and other perioperative outcomes with emphasis on sex differences.

All results were categorized according to the different surgical approaches (coronary artery bypass grafting(CABG) surgery, valvular surgery, combined cardiac surgery(CABG and valvular surgery), and TAVR.

After initial selection, the references of the included articles were reviewed to find additional relevant publications. Of the remaining articles, the title and abstract were screened by three independent reviewers to ensure they met the inclusion criteria. After this selection, the full-text articles were checked for quality before final inclusion.

The risk of bias was assessed using the ROBINS-1 tool (21). Articles with serious judgments were discussed separately among the independent researchers to determine their suitability for

TABLE 1 LV relaxation, filling pressures, 2D and Doppler findings associated with different grades of LVDD, based on American society of echocardiography and European association of cardiovascular imaging standards (2).

| Measurement | Normal | HFpEF | | |
		LVDD grade I	LVDD grade II	LVDD grade III
Left ventricular relaxation	Normal	Impaired	Impaired	Impaired
Mean left atrial Pressure	Normal	Low or normal	Elevated	Elevated
Mitral E/A ratio	≥0.8	≤0.8	>0.8–<2	>2
Average E/e' ratio	<10	<10	10–14	>14
Peak tricuspid regurgitation velocity (m/s)	<2.8	<2.8	>2.8	>2.8
Left atrial volume index	Normal	Normal or increased	Increased	Increased

HFpEF, heart failure with preserved ejection fraction; LVDD, left ventricular diastolic dysfunction.

inclusion. The PRISMA guidelines were used in the writing of this review.

Results

We identified 397 articles from the primary search, an additional 57 were included after checking references, 107 resulting in a total of 454 articles. After the removal of duplicates, a total of 412 records remained for further 108 screening. After screening by title and abstract, 372 articles were excluded, the remaining 20 articles 109 underwent a full-text assessment. Finally, 19 articles were included in this review, with a total of 104.325 patients (33.0% female) (Table 2).

Early (<30 day) mortality

CABG surgery

Three articles (Sun et al., Dalén et al., and Merello et al.,) evaluated 30-day mortality after on-pump CABG in 82.180 (31.5% female) patients (22–24). Dalén et al., showed that patients with LVDD grade I/II/III had a higher risk of early mortality, compared to patients with LVDD grade 0[HR 1.83, 95% CI (1.26, 2.66)]. Additionally, Merello et al., confirmed this finding: patients with LVDD grade II/III had a higher risk of 30-day mortality compared to patients with LVDD grade 0/I/II[OR 20.9, 95% CI (5.5, 78.9), $p = .018$].

Sun et al. did not include study patients with LVDD, but focused on patients with HFpEF(EF >50%) and found this group had higher 30-day mortality after on-pump CABG, than patients with Heart Failure with Reduced Ejection Fraction(HFrEF) (Hazard Ratio(HR) 2.57, 95% CI [1.96, 3.36] (22).

Only Sun et al., and Merello et al., analyzed data on sex differences. Sun et al., showed that females with HFpEF had a higher 30-day mortality compared to males with HFpEF(HR 2.89, 95% CI [1.91, 4.37] vs. HR 2.32, 95% CI [1.62, 2.34]) (22). In contrast, Merello et al., observed that female sex was not an independent predictor of 30-day mortality in patients with LVDD undergoing CABG[OR 1.7, 95% CI (0.5, 5.4), $p = .376$] (24). However, the latter study was substantially smaller than the previous two studies.

Valvular surgery

Chang et al., investigated 30-day mortality in 210 patients with LVDD grade III, who underwent surgical aortic valve replacement (AVR) (26). None of the patients died within 30 days, so sex differences in mortality were not analyzed.

Combined cardiac surgery

Five studies reported on in-hospital mortality in patients undergoing combined cardiac surgery (20, 28, 30, 33, 34). Salem et al., showed that a LVEDP ≥19 mmHg was associated with a significantly higher risk of in-hospital mortality and independent of LVEF [OR 1.19, 95% CI (1.05, 1.35), $p = .0062$] (34).

Nguyen et al., demonstrated that LVDD grade I/II/III was predictive of in-hospital mortality after cardiac surgery, independent of the EuroSCORE II [HRadj: 1.6, 95% CI (1.0, 2.6), $p = .049$] (33). This was also the conclusion of Metkus et al., and Beaubien-Souligny et al., In the results of Metkus et al., LVDD grades II/III were significantly predictive of in-hospital mortality ($p = .004$), as were those of Beaubien-Souligny et al. In the latter study, LVDD grade III was significantly associated with an increased risk of in-hospital mortality after cardiac surgery, compared to patients without LVDD [OR 19.39, 95% CI (2.37, 158.48), $p = .006$] (20, 30).

A solitary study demonstrated the exact opposite. Ferreira et al., reported that none of the following were significant predictors of in-hospital mortality after cardiac surgery: female sex, LVDD or E/e' levels ($p = .62$, $p = .11$, and $p = .24$, respectively) (28).

TAVR

The only study concerning TAVR, Krittanawong et al., found no difference in in-hospital mortality between patients with HFpEF vs. patients with HFrEF (3.17% vs. 3.66%; $p = .35$) (35). No analysis was done on the comparison LVDD vs. no LVDD regarding in-hospital mortality. Sex was not significantly associated with mortality in the HF cohorts (HFpEF and HFrEF).

Early(≤30-day) postoperative complications and morbidity

CABG surgery

Merello et al., reported on the early complication rate among 191 patients undergoing on-pump CABG (24). They found a significantly higher incidence of the following complications in patients with LVDD grade III, compared to patients with LVDD grade 0/I/II: low cardiac output ($p = .009$), acute renal failure ($p < .001$), longer duration of mechanical ventilation ($p < .001$), and overall complication rate ($p = .01$). No data were available on the association between female sex and these early complications.

Lee et al., and Youn et al., examined the early complication rate in 2,304 patients undergoing off-pump CABG (36, 39). Lee et al., reported that patients with LVDD grade III were independently associated with a higher percentage of 30-day Major Adverse Cardiovascular Events (MACE) [OR 2.4, 95% CI (1.4–3.9), $p = .001$], while Youn et al., stated that no significant difference was found in 30-day MACE ($p = .23$) among patients with different LVDD grades. However, in the same study, multivariate analysis revealed that LVDD grade II/III independently predicted respiratory complications [OR 3.68, 95% CI (1.84–20.36), $p = .01$]. Early morbidity was also studied by Jun et al., in 500 patients undergoing off-pump CABG (38). They showed that a LVDD grade III, before off-pump CABG, was significantly associated with a higher risk of postoperative morbidity, compared to patients without LVDD[OR 2.42, 95% CI (1.42, 4.14), $p < .005$].

TABLE 2 Overview of the included articles with their relevant outcomes ordered by the procedure performed.

Study (year)	Number of patients (n)	♀ (%)	Method of assessing diastolic function	Type of surgery	Relevant outcomes
Sun et al. (22)	40.083	31.7%	Not specified	CABG	Primary: death from any cause (≤30 days)
Dalén et al. (23)	41.906	31.3%	Not specified	CABG*	Primary: death from any cause
					Secondary: combination of all-cause mortality
Merello et al. (24)	191	29.1%	Preoperative TTE	CABG	Primary: in-hospital mortality, mortality and complications (≤30 days)
Değirmencioğlu et al. (25)	472	26.6%	Not specified	CABG	Primary: need for perioperative inotropic support (>4 h) POAF, HLOS, mortality (≤30 days)
Chang et al. (26)	210	35.2%	Preoperative, TDI	AVR	Primary: in-hospital cardiovascular events
					Secondary: mortality (≤30 days)
Groban et al. (27)	205	25.4%	Intraoperative, TEE	CABG, valvular, CABG + valvular	Primary: ICULOS, HLOS, MV duration, use of inotropic support
Ferreira et al. (28)	153	34.0%	Intraoperative, TEE	CABG, CABG + AVR, CABG + MVR	Primary: in-hospital mortality
					Secondary: ICULOS and HLOS
Kyle et al. (29)	121	19.0%	Intraoperative, TEE	CABG, valvular, CABG + valvular	Primary: CPOMS at day 3, 5, 8 and 15.
					Secondary: ICULOS, HLOS, POAF
Beaubien-Souligny et al. (30)	760	26.7%	Preoperative, TEE	CABG, valvular, multiple procedures	Primary: in-hospital mortality
					Secondary: DSB, ICULOS, HLOS
Bernard et al. (31)	66	33.3%	Preoperative, TEE	CABG, valvular, CABG + AVR, CABG + MVR, CABG + AVR + MVR, reoperations	Primary: DSB, need for postoperative vasoactive support
Melduni et al. (32)	351	32.8%	Preoperative, TTE	CABG, valvular, CABG + valvular	Primary: POAF
Metkus et al. (20)	577	27.7%	Preoperative, TTE	CABG, AVR, CABG + AVR	Primary: death (≤30 days), prolonged MV, ICU readmission during hospitalization, HLOS (>14 days)
Nguyen et al. (33)	1.743	29.0%	Not specified	CABG, valvular surgery, thoracic aorta surgery	Primary: in-hospital mortality
					Secondary: Postoperative need for inotropic support (<24 h)
Salem et al. (34)	3.024	28.4%	Not specified	CABG, valvular, multivalvular, valvular surgery + CABG, thoracic aorta aneurysm surgery	Primary: in-hospital mortality
Krittanawong et al. (35)	11.609	47.5%	Not specified	TAVR	Primary: in-hospital mortality
Lee et al. (36)	1.048	24.6%	Not specified	Off-pump CABG	Primary: 30-day MACE
Shim et al. (37)	50	32.0%	Preoperative, TTE	Off-pump CABG	Primary: ICULOS
Jun et al. (38)	500	31.6%	Preoperative, TTE	Off-pump CABG	Primary: postoperative morbidity during hospitalization, in-hospital mortality
Youn et al. (39)	1.256	28.2%	Preoperative, TTE	Off-pump CABG	Primary: MACE
					Secondary: postoperative complications

LVDD, left ventricular dysfunction; CABG, coronary artery bypass grafting; HF, heart failure; TDI, tissue Doppler imaging; AVR, aortic valve replacement; POAF, post-operative atrial fibrillation; HLOS, hospital length of stay; ICULOS, intensive care length of stay; MV, mechanical ventilation; MVR, mitral valve replacement; TEE, transesophageal echocardiogram; TTE, transthoracic echocardiogram; CPOMS, cardiac postoperative morbidity score; DSB, difficult separation from cardiopulmonary bypass; ICU, intensive care unit; TAVR, transcatheter aortic valve replacement; DD, diastolic dysfunction; MACE, major adverse cardiac events.
*Off-pump CABG in 3.7% of the patients.

None of the studies reported on sex-differences regarding early postoperative morbidity and complications.

Combined cardiac surgery

Two studies evaluated early complications in 472 patients during combined cardiac surgeries (CABG, valvular, or CABG + valvular combined) (29, 32). Kyle et al., showed in 121 patients that LVDD (grade unspecified) correlated with new-onset POAF, compared to patients without LVDD [OR 4.50, 95% CI (1.22, 25.17), $p = .016$]. Thus, each grade of LVDD was associated with a higher Cardiac Postoperative Morbidity Score (CPOMS) on day 5(4.73 ± 7.18 vs. 3.04 ± 2.31; $p = .009$) and day 8($5.23 \pm$ 8.62 vs. 2.83 ± 7.76; $p = .009$) compared to patients without LVDD. In addition, the overall CPOMS was 1.14 points higher ($p = .01$) after adjustment for potential confounders. Similarly, Melduni et al., demonstrated that higher grades of LVDD were significantly associated with an increased incidence of POAF, compared to patients without LVDD [grade I: OR 9.9, 95% CI (3.41, 29.8), $p < .001$], grade II: [OR 22.2, 95% CI (7.69, 63.8), $p < .001$], grade III: [OR 45.5, 95% CI (12.0, 173.0), $p < .001$] (32).

There were no studies that provided information about sex-based disparities in terms of early postoperative morbidity and complications.

HLOS and ICULOS

CABG surgery

Merello et al., demonstrated that HLOS for patients undergoing on-pump CABG was significantly longer in patients with LVDD grade III, compared with patients with LVDD grade 0/I/II(13 vs. 8 days, respectively) (24). In contrast, Değirmencioğlu et al., reported no significant difference in HLOS after on-pump CABG in patients with mild LVDD (grade I), compared with patients without LVDD (6.57 ± 0.14d vs. 7.19 ± 0.45d) (25). There was also no significant difference in ICULOS (26.2 ± 1.9 h vs. 24.1 ± 1.4 h).

No research findings indicated any distinctions between sexes concerning regarding HLOS and ICU.

In off-pump CABG, Lee et al., and Shim et al., showed that patients with LVDD grade III underwent prolonged ICULOS compared to patients with LVDD grade I/II, and without LVDD ($p = 0.003$ and $p = 0.004$, respectively) (36, 37). In addition, Lee et al., reported that LVDD grade III was also predictive of prolonged HLOS, compared to LVDD grade I/II ($p < .001$). No data on sex-differences regarding HLOS and ICULOS were reported in these two studies. A third study by Youn et al., noted that patients with LVDD grade III had a higher risk of HLOS >12 days, compared with patients without LVDD [OR 5.75, 95% CI (1.81, 13.23), $p < .01$] (39). Multivariate logistic regression showed that female sex was predictive of HLOS >12 days after off-pump CABG ($p < .01$).

Combined cardiac surgery

Five studies evaluated ICULOS and HLOS after combined cardiac surgery. Groban et al., found LVDD grade I-III were independently associated with prolonged ICULOS in patients undergoing CABG, valvular, or CABG with valvular surgery ($p = .037$) (27). This association was also confirmed by Ferreira et al., who reported that higher E/e' ratios were predictive of prolonged ICULOS ($p = .009$) but not HLOS ($p = .086$) (28). Kyle et al., demonstrated that any grade of LVDD was significantly associated with longer ICULOS compared to patients without LVDD ($p = .019$) (29). Furthermore, Beaubien-Souligny et al., showed that LVDD grade II/III was significantly associated with longer ICULOS compared to patients without LVDD, or grade I ($p = .002$ and $p < .001$) and additionally that LVDD grade III was related to longer HLOS, compared to patients without LVDD ($p = .02$) (30). Metkus et al., added that higher grades of LVDD were predictive of longer HLOS (grade 0: 9 (7–13) days vs. grade I: 10(8–14) days vs. grade II: 11(7–17) days vs. grade III: 20.5 (12.5–24) days) ($p = .0001$) (20).

One study reported on sex differences in ICULOS and HLOS after combined cardiac surgery. Ferreira et al., reported that female sex was independently associated with a two-fold higher risk of prolonged HLOS[IHR 2.27, 95% CI (1.55, 3.32), $p < .001$] and increased ICULOS[IHR 1.73, 95% CI (1.20, 2.49), $p < .017$]. However, they found no significant association between LVDD and prolonged HLOS or ICULOS ($p = .232$ and $p = .318$) (28).

Other sex-related perioperative outcomes

Ferreira et al., demonstrated that patients with elevated LV filling pressures (E/e' ≥ 8) were more often female ($p < .01$), and that females had significantly higher LVDD grades ($p < .01$) (28). Bernard et al., pointed out that female sex, together with LVDD, predicted an increased inotropic need [OR 8.44, 95% CI (2.09, 42.09), $p = .004$], and difficult separation from cardiopulmonary bypass ($p = .004$) (31). No subgroup analysis of LVDD grading was made.

Discussion

This review aimed to investigate the impact of LVDD on early outcomes such as mortality, morbidity, complications, HLOS, and ICULOS after cardiac surgery and percutaneous aortic valve procedures, focusing on sex disparity.

Female sex was revealed to be significantly associated with higher LVDD grades and E/e' ratios at baseline in patients undergoing cardiac surgery. Females with LVDD presented with increased LVEDP, twice the risk of prolonged HLOS, increased ICULOS, increased need for inotropic support up to 12 h after surgery, and difficult separation from cardiopulmonary bypass. In addition, after off-pump CABG, females with LVDD showed significantly longer HLOS compared to males with LVDD.

Concerning LVDD and HLOS or ICULOS, however, there is some inconsistency in the literature. While studies by Metkus et al., Kyle et al., and Beaubien-Souligny et al. (20, 29, 30) indicated significant correlations between LVDD and extended HLOS and ICULOS, Ferreira et al., reported no notable link between the same variables (28). Interestingly, the latter study revealed an independent association between female sex and an almost twofold increase in the risk of extended HLOS and ICULOS. The inconsistency in results might be due to the absence of sex-based stratification in the three studies that showed a significant connection between LVDD and prolonged HLOS and ICULOS. In contrast, Ferreira et al., analyzed results by sex and identified an independent association between female sex and prolonged ICULOS or HLOS.

Concerning mortality, no significant association was found between female sex and in-hospital mortality after on-pump cardiac surgery. Results regarding the effect of female sex on early mortality (≤ 30 days) after on-pump CABG surgery, however, were inconsistent; Sun et al., reported female sex was associated with higher early mortality in LVDD patients (22), while Merello et al., found that female sex was not an independent predictor of 30-day mortality (24). There are different reasons for this inconsistency. This discrepancy could be attributed to the varying baseline characteristics of the included patients. Patients in the study of Sun et al., were older (mean age difference: 7.6 years) and were more likely to have a history of hypertension(95.4% vs. 71.1%), COPD (40.5% vs. 0.4%), DM (59.9% vs. 34.6%) or obesity (32.9% vs. 10.0%), compared with patients in the study by Merello et al. These factors already confer a higher *a priori* risk of increased 30-day mortality in the study by Sun et al. (22). Furthermore, the study carried out by Merello et al., featured a notably smaller sample size, resulting in a decrease in statistical power. Therefore, although the

study result was statistically non-significant, it is still compatible with an increased mortality risk, which would be clinically relevant.

The outcomes concerning predictors of in-hospital mortality, following on-pump cardiac surgery, were largely consistent. Four studies identified three predictors of in-hospital mortality after on-pump cardiac surgery: LVDD, LVEDP ≥19 mmHg, and higher LVDD grades (20, 30, 33, 34). In contrast, although the study by Ferreira et al., showed that females were more likely to present with higher grades of LVDD before on-pump cardiac surgery, they found no significant association between female sex, LVDD, or E/e' values and in-hospital mortality (28). It is possible that the baseline characteristics of patients in the study by Ferreira et al., might have been more favorable concerning comorbidities than those in the studies by Metkus et al., Beaubien-Souligny et al., Nguyen et al., and Salem et al. (20, 30, 33, 34). Another explanation might be that the study by Ferreira et al., has a considerably smaller study population ($n = 153$) vs. Beaubien-Souligny et al. ($n = 760$), Metkus et al. ($n = 577$), Nguyen et al. ($n = 1,743$), and Salem et al. ($n = 3,024$), and may thus be underpowered to detect any differences in these outcomes.

Limitations

Our literature review had different limitations. Firstly, there was no uniform definition of LVDD in the included studies. Various combinations of echocardiography parameters and different cutoff values were used to determine the LVDD grade, making it more difficult to compare results directly. This is probably due to the fact that part of the included studies predate the 2016 guideline from the American Society of Echocardiography and the European Association of Cardiovascular Imaging, which shifted the focus away from volume status-dependent parameters to the consequences of diastolic impairment, such as left atrial volume. Secondly, the timing and imaging modalities used to determine LVDD differed between studies, as this was assessed either preoperatively, intraoperatively, or perioperatively and either by transesophageal echocardiography (TEE) or transthoracic echocardiography (TTE). Importantly, it should be noted that intraoperative assessment of LVDD may have been affected by factors such as anesthetic medication, inotropic and vasoactive medication, and positive pressure ventilation. By including these studies in our review, we assumed that preoperatively diagnosed LVDD has the same impact on early postoperative outcomes after cardiac surgery, as LVDD identified during the intraoperative phase. Furthermore, due to the heterogeneity of cardiac surgical procedures and the variation in study outcomes, comparing results with a conclusive statement is difficult.

Strength

The strength of our review is a systematic approach including the ROBINS-I tool we used to assess the available literature. Selection bias was minimized by including independent reviewers in identifying articles. In addition, we only included studies with higher-quality evidence, such as randomized controlled trials and observational studies. Finally, the authors of the included articles attempted to adjust for baseline characteristics. Thus, outcomes

among patients with LVDD who underwent cardiac surgery were more comparable by differentiating underlying differences in baseline characteristics.

Future

Further research is essential to address the open questions surrounding LVDD. Previous studies have shown that females are at a higher risk of LVDD than males, yet the studies in this review included fewer female participants than males. To improve future study methodology, additional research should assess LVDD at a standardized moment (e.g., pre-operative phase) utilizing an uniform standard of LVDD grading, conduct subgroup analysis or stratification by sex, adjusting for baseline differences, and differentiate outcomes by cardiac surgical procedures. A follow-up study can help identify specific therapies to manage intraoperative LVDD and minimize the risk of poorer outcomes in females.

Conclusion

Despite the limited number of studies focusing on sex differences, females with LVDD appear to have worse early outcomes (≤30 days) after cardiac surgery, compared to men. Future research will need to identify sex-specific risk factors and target treatment optimization.

Author contributions

TL: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Writing – original draft, Writing – review & editing. TA: Writing – review & editing. JB: Formal analysis, Investigation, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. EK: Methodology, Supervision, Writing – review & editing. SJ: Conceptualization, Formal analysis, Methodology, Writing – original draft. SB: Writing – review & editing. JH: Writing – review & editing. HH: Writing – review & editing. SE: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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