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ORIGINAL ARTICLE

Preexisting heart failure is an underestimated risk factor in cardiac surgery

K. A. Kortekaas · J. H. N. Lindeman · M. I. M. Versteegh · T. Stijnen · R. A. E. Dion · R. J. M. Klautz

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Abstract
Background Heart failure is characterised as a strong risk factor for systemic failure after cardiac surgery. However, the impact has never been substantiated.
Methods Patients with heart failure (n=48) - scheduled for elective ventricular reconstruction or external constraint device-were compared with a one-to-one matched control group of patients without heart failure undergoing cardiac surgery between 2006 and 2009.
Results As expected, patients with heart failure more frequently experienced complications definitely related to pump failure (p=0.01). However, complications not related to their pump failure were also more often observed, such as prolonged mechanical ventilation, sepsis and vasoplegia (p=0.01). Overall, organ dysfunction-circulatory, renal, and pulmonary failure-was often observed in heart failure patients, contributing to a prolonged stay in the intensive care unit (p<0.001) as well as in hospital (p=0.01).
Conclusion The adverse postoperative course in patients with heart failure is not only directly related to circulatory failure, but merely reflects a systemic dysregulation. Our findings suggest that heart failure impacts outcome and should therefore be included in prevailing risk classification systems. Offensive perioperative treatment strategies, focused on the main complications in patients with heart failure, will lead to improved results after cardiac surgery.

Keywords Cardiac surgery · Complications · Heart failure

Introduction

Heart failure is one of the most common, costly, disabling, and potentially deadly pathologies worldwide [1, 2]. Ageing of the population and improved treatments of the causes of heart failure will lead to an increased incidence and prevalence of heart failure. Due to the limited availability of donor organs, heart transplantation is only an option for very few patients. Alternative surgical therapies are important and aimed at improving the myocardial function.

Although the efficacy of several surgical interventions has been established for patients with heart failure [3–5], perioperative morbidity and mortality remain significant and hamper widespread use. The observed complications can not only be explained by the preoperative high risk state of the patient or the low cardiac output state alone. They are rather explained by systemic responses such as vasoplegia and 'a' systemic inflammatory response syndrome.

Our hypothesis is that postoperative complications in patients with preexisting heart failure are often not related to pump failure. In other words, the preoperative risk

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K. A. Kortekaas · M. I. M. Versteegh · R. J. M. Klautz (✉)
Department of Cardiothoracic Surgery,
Leiden University Medical Center,
K6-S, PO Box 9600, 2300, RC Leiden, the Netherlands
e-mail: r.j.m.klautz@lumc.nl

K. A. Kortekaas
e-mail: k.a.kortekaas@lumc.nl

J. H. N. Lindeman
Department of Vascular Surgery,
Leiden University Medical Center,
Leiden, the Netherlands

T. Stijnen
Department of Statistics and Bioinformatics,
Leiden University Medical Center,
Leiden, the Netherlands

R. A. E. Dion
Department of Cardiothoracic Surgery, Ziekenhuis Oost-Limburg,
Genk, Belgium

stratification, which only includes ejection fraction as a measure of pump failure, is inadequate to predict an adverse postoperative course. To test this hypothesis, we compared patients with and without heart failure undergoing cardiac surgery in order to have comparable surgical injury. Our aim was to systematically examine the impact of preexisting heart failure on complications after correction for pump failure by differentiating between complications not, possibly or definitely related to pump failure.

Methods

Patient characteristics

Between January 2006 and December 2009, all patients with preexisting heart failure scheduled for an elective external cardiac support device or ventricular reconstruction were included in this retrospective study (n=48). Heart failure was defined as an inadequate pump function of the heart with an echocardiographically estimated ejection fraction biplane <30% and New York Heart Association (NYHA) class III or IV. Exclusion criteria were minimal access procedures, previous sternotomy, emergency procedures or heart failure hospitalisation prior to admission to our department. Hospitalisation is often an indication for an aggravated acute state of heart failure, affecting outcomes. All patients were scheduled for a restrictive mitral annuloplasty in addition to their external constraint device or ventricular reconstruction. To examine the impact of heart failure on adverse outcomes, all 48 heart failure patients were matched on a one-to-one basis with patients without heart failure undergoing cardiac surgery (controls). All 48 controls had a normal pump function (ejection fraction biplane ≥50%) and presented in NYHA class I or II. Each patient with heart failure was first matched for gender and year of surgery, and then for the most closely resembling age. Controls were scheduled for at least reconstructive mitral valve surgery to limit heterogeneity and to have a comparable duration of surgery between the groups. Moreover, mitral valve surgery is a common procedure in both patients with and without heart failure [6–8]. Our study protocol was approved by the local ethics committee, who waived the need for individual informed consent due to the retrospective and anonymous nature of the study.

Performed surgical procedures

Surgical procedures were performed according to the local standard. An external cardiac support device (CorCap cardiac support device, Acorn Cardiovascular, St. Paul, Minnesota) was placed if a left ventricular end-diastolic diameter above 65 mm was measured on the preoperative echocardiographic examination. Patients were considered eligible for ventricular reconstruction as described by Dor et al. [9] if they had a large area of anterior akinesia or dyskinesia [10]. Tricuspid valve annuloplasty, coronary artery bypass grafting and ablation procedures were performed if indicated.

Endpoints and data collection

The complicated course of patients with heart failure is of high interest in current pathophysiological investigations. Complications, with often unravelled aetiology, were categorised prior to the start of our study and were based on the opinion of experts in the field of heart failure surgery, i.e. cardiac surgeons and intensivists. Primary endpoints were a composite of complications not, possibly and definitely related to pump failure in an attempt to differentiate between pump failure and systemic failure. Secondary endpoints included the individual components of these primary endpoints in addition to other complications (Table 1). Patients were followed until discharge from hospital or death. Mortality was compared with a preoperative risk-adjusted model (logistic EuroSCORE) [11–13]. Data collection was performed by examination of the patients' electronic or hard copy medical records of standard postoperative procedures, or by interviewing their general practitioner by telephone. Serum creatinine levels (Roche Diagnostics, Mannheim, Germany) were assessed within 3 months prior to surgery and blood pressure was measured the day before surgery. Excessive bleeding was defined as blood loss of more than 2 liters within 24 hours postoperatively [14].

Statistical analysis

The occurrences of the primary and secondary endpoints were compared between the two patient groups. All statistical analyses were performed with the Statistical Package for the Social Sciences 17.0 (SPSS Inc., Chicago, IL, US). Continuous variables were expressed as mean±standard deviation (SD) and categorical data as number of patients. Continuous variables were analysed with the unpaired t-test or the Mann–Whitney U where appropriate, and categorical variables with a chi-square test.

Results

Patient characteristics

Baseline patient variables and an overview of surgical procedures are shown in Table 2 and the supplementary data, respectively. Equal age and gender distribution reflect the matching process. As expected, patients with heart failure had a higher logistic EuroSCORE and NYHA functional

Table 1 Definitions of the primary and secondary endpoints

Composite endpoints	
Not related to pump failure	Mechanical ventilation ≥48 hours, sepsis and vasoplegia (norepinephrine ≥0.2 μg/kg/min, 12–24 hours in the ICU); 2 or 3 present
Possibly related to pump failure	Early mortality and acute kidney injury; both present
Definitely related to pump failure	Inotropic support (dobutamine ≥5 μg/kg/min, 12–24 hours in the ICU) and use of mechanical assist devices (intra-aortic balloon pump or ventricular assist device); both present
Mortality	
Early mortality	All-cause mortality occurring within 30 days or in hospital [12]
Late mortality	All-cause mortality occurring from 30 days or in hospital to 1 year [12]
Organ dysfunction	
Circulatory failure	Use of an intra-aortic balloon pump or use of a ventricular assist device
Neurological events	Transient ischaemic attack (fully reversible symptoms of short duration), stroke (neurological deficit persisting ≥72 hours) confirmed by clinical findings and computed tomography scan, and documented critical illness neuropathy
Renal failure	Acute kidney injury (50% increase in creatinine values ≤48 hours postoperatively [17] and/or a postoperative creatinine value ≥200 μmol/L) and use of continuous venovenous haemofiltration
Pulmonary complications	Mechanical ventilation ≥48 hours, re-intubation, tracheostoma, ventilator-associated pneumonia or pneumothorax
Sepsis	Clinical suspicion confirmed by a positive blood culture (gold standard)

class. Heart failure patients had lower blood pressure values and higher creatinine values at baseline.

Primary endpoints

The three primary endpoints are listed in Table 3. The composite endpoint of complications not related to pump failure was observed more frequently in patients with heart failure (p=0.01). In detail, this first endpoint was observed in 10/48 heart failure patients (20.8%) and 0/48 controls (0.0%). Secondly, the composite endpoint of complications possibly related to pump failure was observed in 6 of the 48 patients with heart failure (12.5%) and in 1 of the 48 controls (2.1%). This second endpoint was, although six times more often, not significantly different between the groups (p=0.12). This result indicates that early mortality and acute kidney injury may be related to pump failure but may also be related to other factors influencing these outcomes. For

Table 2 Baseline variables of patients with heart failure (HF) and controls

	HF (n=48)	Controls (n=48)	p value
Clinical characteristics			
Age (years)	62.6±9.3	62.5±8.2	0.96
Gender (male/female)	39/9	39/9	1.00
Diabetes mellitus (no. of patients)			
Insulin dependent	7 (14.6%)	2 (4.2%)	0.16
Non-insulin dependent	6 (12.5%)	4 (8.3%)	0.74
NYHA functional class	3.1±0.3	1.7±0.5	<0.001
MI <3 months prior to surgery (no. of patients)	1	0	1.00
Significant CAD (no. of patients)	28	19	0.10
Logistic EuroSCORE (%)	10.4±6.3	3.3±2.1	<0.001
Systolic blood pressure (mmHg)	113.0±17.7	133.6±18.8	<0.001
Serum creatinine (μmol/L)	114.4±38.7	90.9±18.4	<0.001
Surgical characteristics			
Duration of surgery (min.)	357.5±107.9	329.6±82.5	0.27
Cardiopulmonary bypass time (min.)	213.1±79.7	192.4±55.5	0.14
Aortic cross clamp time (min.)	134.3±58.2	146.8±51.0	0.16

Details noted as mean ± SD; *CAD* coronary artery disease; *MI* myocardial infarction

Table 3 Postoperative outcomes of patients with heart failure (HF) and controls

Postoperative outcomes (no. of patients)	HF (n=48)	Controls (n=48)	p value
Composite endpoints			
Not related to pump failure	10	0	0.01
Possibly related to pump failure	6	1	0.12
Definitely related to pump failure	8	0	0.01
Mortality			
Early mortality	8	1	0.04
Late mortality	3	1	0.61
Organ dysfunction			
Circulatory failure: mechanical assist devices	19	0	<0.001
Neurological events			
Transient ischaemic attack	0	1	1.00
Stroke	1	1	1.00
Documented critical illness neuropathy	5	1	0.06
Renal failure			
Acute kidney injury	10	5	0.24
Continuous venovenous haemofiltration	8	1	0.03
Pulmonary complications			
Mechanical ventilation ≥48 hours	13	4	0.03
Reintubation	4	2	0.65
Tracheostoma	1	0	1.00
Ventilator-associated pneumonia	12	3	0.02
Pneumothorax	2	0	0.47
Sepsis	7	1	0.06
Pharmacological support 12–24 hours at the ICU			
Norepinephrine ≥0.2 μg/kg/min	11	0	0.001
Dobutamine ≥5 μg/kg/min	16	3	0.002

example, acute kidney injury may also be drug-induced during the perioperative period. Thirdly, the composite endpoint of complications definitely related to pump failure was, as expected, significantly different between the groups (p=0.01). This last endpoint occurred in 8/48 heart failure patients (16.7%) and in 0/48 controls (0%).

Secondary endpoints

Secondary endpoints are shown in Table 3. Early mortality was more common in heart failure patients as compared with controls (8/48 patients (16.7%) versus 1/48 patients (2.1%), respectively). One heart failure patient died in the operating room due to circulatory failure after ventricular reconstruction. In both groups the primary causes of early mortality were septic and cardiogenic shock. Surprisingly, the early mortality in patients with heart failure exceeded the predicted mortality based on the logistic EuroSCORE (10.4%), while in the controls the early mortality was lower than the predicted mortality (3.3%). Late mortality was similar between the groups: 3/48 patients with heart failure (6.3%) and 1/48 controls (2.1%). Those three heart failure patients died as a result of terminal or acute heart failure. The cause of late mortality of the control patient is unknown.

Organ dysfunction was divided into circulatory failure, neurological events, renal failure and pulmonary complications. Circulatory failure was more often observed in patients with heart failure, as expected due to their pump failure. These patients more often needed an intra-aortic balloon pump as a temporary cardiac assist device. The occurrence of neurological events was similar between the groups. The incidence of acute kidney injury was higher, although not significant, in patients with heart failure as compared with controls. Use of renal replacement therapy was strongly associated with mortality: 5/8 heart failure patients who needed continuous venovenous haemofiltration died in hospital. Also the control patient who died early needed dialysis. Prolonged ventilatory support (≥48 hours) and ventilator-associated pneumonias were more often observed in patients with heart failure. The more complex postoperative course for patients with heart failure was also reflected by the use of high concentrations of norepinephrine to treat vasoplegia and dobutamine as inotropic support. Overall, organ dysfunction was frequently observed in heart failure patients, contributing to a prolonged stay in the

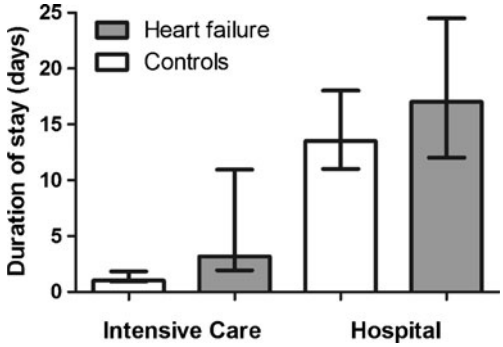

Fig. 1 Intensive care unit stay and total stay in hospital of patients with preexisting heart failure and controls. Patients with preexisting heart failure experienced a longer stay at the intensive care unit ($p<0.001$) than controls (median ± interquartile range of 3.2 (1.9–11.0) versus 1.0 (0.9–1.8)). In addition, they experienced a longer total stay in hospital ($p=0.01$) than controls (median ± interquartile range of 17.0 (12.0–24.0) versus 13.5 (11.0–18.0))

intensive care unit ($p<0.001$) as well as a longer total stay in hospital ($p=0.01$; Fig. 1).

The number of patients with excessive bleeding postoperatively was similar between the groups ($p=0.98$); three heart failure patients versus two controls. Early and late re-explorations for excessive bleeding or tamponade were similar in both groups (one early and one late re-exploration in patients with heart failure versus two early and two late re-explorations in the controls, both $p=1.00$). All patients with a late pericardial tamponade could be treated by pericardial puncture. Patients with heart failure underwent a reoperation five times more often, although this was not significant ($n=5$ versus $n=0$, respectively, $p=0.07$).

Discussion

This study confirms the clinical observation that preexisting heart failure is a risk factor for systemic dysregulation after cardiac surgery. Not all adverse outcomes were related to the insufficient pumping capacity of the heart itself but merely to a cluster of organ dysfunction, suggesting systemic dysregulation. In an attempt to differentiate between pump failure and systemic failure, three composite endpoints were determined. As expected, the composite endpoint of complications definitely related to pump failure was significantly different between the groups. The composite endpoint of complications possibly related to pump failure-containing early mortality and acute kidney injury-was, however, not significantly different. This could first of all be the result of the relatively small patient numbers in this study, because this endpoint was observed six times more often in patients with heart failure. Moreover, during the postoperative period the serum creatinine values to assess acute kidney injury may not be accurate because of imbalances between creatinine production and elimination. Most interestingly to support our hypothesis was the composite endpoint of complications not related to pump failure. This endpoint was observed ten times more often in patients with heart failure, indicating systemic dysregulation.

The early mortality in patients with heart failure was higher than the preoperative expected mortality, based on the logistic EuroSCORE; while in the controls the early mortality was lower than the predicted mortality. In our opinion, the syndrome of heart failure is underestimated when using the logistic EuroSCORE to predict the mortality of patients with heart failure. This can be explained by the way the EuroSCORE was established [11]. There is an additive effect of heart failure on mortality, which is not well represented by only the ejection fraction in this scoring system. This suggests that heart failure surgery needs a modified risk stratification system. It is also the question if there were enough patients with heart failure included in the data collection for the development of the new version of the EuroSCORE system.

In this study it became clear that heart failure patients more often experience a systemic dysregulation postoperatively. The prolonged intensive care unit stay and total stay in hospital are mainly caused by sepsis, vasoplegia, prolonged mechanical ventilation with ventilator-associated pneumonias as a result, and organ dysfunction in general. The exact mechanisms of these outcomes are not yet unravelled, but were not directly related to the insufficient pumping capacity of the heart. Systemic disturbances are recognised to contribute to patient morbidity and mortality after cardiac surgery [15]. Those disturbances may comprise complement activation, immune cell activation, oxidative stress and others in addition to inflammation. One of the underlying mechanisms might be the different response to ischaemia/reperfusion injury. In our opinion, this nearly inevitable phenomenon in cardiac surgery on top of susceptible vascular beds in patients with heart failure might be the cause of the observed systemic dysregulation. However, further research is needed to assess the individual contribution of those underlying pathophysiological mechanisms to the observed systemic dysregulation.

Some issues merit mention. Patients with preexisting heart failure were frequently hospitalised prior to admission to our department. Although they are usually hospitalised at least once for adaptation of the treatment before they are considered for surgery, hospitalisation in the days prior to surgery is often seen in patients with acute heart failure. In our opinion, including these patients would give an overestimation of the primary and secondary endpoints. However, excluding these hospitalised patients contributed to the relatively small patient numbers. Baseline differences for systolic blood pressures between the groups may reflect pharmacological treatment, because the therapy for heart failure is aimed at lowering the blood pressure with β-

blockers and ACE inhibitors. The logistic EuroSCORE identified various preoperative risk factors related to mortality, but none of our statistically different baseline variables between the two groups are included in this scoring system. Compared with a study by Conlon et al. [16], our percentages of patients requiring renal replacement therapy are relatively high, but are influenced by local policy to treat acute kidney injury early and aggressively to prevent further deterioration of the kidney function.

Conclusion

This study shows that the majority of observed complications in patients with preexisting heart failure are not directly related to the insufficient pumping capacity of the heart, but merely reflect a systemic dysregulation. Further research is necessary to unravel underlying mechanisms for this adverse postoperative course. Moreover, the great impact of heart failure on adverse outcomes emphasises the importance of adapting current risk stratification systems, such as the EuroSCORE. Offensive perioperative treatment strategies focused on the described complications will lead to improved results for patients with heart failure after cardiac surgery.

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