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ORIGINAL ARTICLE

# Right ventricular failure after implantation of a continuous-flow left ventricular assist device: early haemodynamic predictors†

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## Abstract

**OBJECTIVES**: Right ventricular failure (RVF) is a significant complication after implantation of a left ventricular assist device. We aimed to identify haemodynamic changes in the early postoperative phase that predicted subsequent development of RVF in a cohort of HeartMate II (HMII) implanted patients.

**METHODS**: This was a single-centre observational study of consecutive placement of HMII devices at Rigshospitalet, Copenhagen. Preoperative data (right heart catheterization, biochemistry and clinical status) and postoperative readings from the first 72 h after implantation (haemodynamics, inotropic and vasoactive therapy) were included in the analysis. The data set was examined for significant differences between patients who developed RVF (RVF group, $n = 11$)—defined as need for inotropic or vasodilator therapy >14 days, nitric oxide therapy ≥48 h or right ventricular assist device therapy—and those who did not (non-RVF group, $n = 22$).

**RESULTS**: Preoperative right heart catheterization data were similar in the two groups. Immediately after HMII implantation, the increase in cardiac index (CI) was significantly larger in the non-RVF than in the RVF group (0.96 ± 0.8 vs 0.2 ± 0.5 L/min, respectively; $P = 0.018$), whereas right ventricular stroke work index (RVSWI) decreased significantly more in the RVF group (−4.3 ± 2.0 vs −0.9 ± 2.0 g m/m$^2$; $P < 0.001$). These differences were present in spite of the RVF group receiving larger doses of catecholaminergic agents ($P = 0.034$). Over the ensuing 72 h, the CI of the RVF group gradually approached that of the non-RVF group; concurrently, however, the differences in inotropic therapy were further enhanced. Pump settings were similar in the two groups.

**CONCLUSIONS**: The haemodynamic alterations characterizing RVF were present already immediately after HMII implantation. RVF development was not related to pump flow and settings.

**Keywords:** Left ventricular assist device • HeartMate II • Postimplantation haemodynamics • Right ventricular failure

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## INTRODUCTION

Right ventricular failure (RVF) remains a major clinical concern early after implantation of left ventricular assist devices (LVAD). The incidence of RVF—usually defined by the need for extended inotropic/vasoactive therapy or a right ventricular assist device (RVAD) [1]—has been reported as high as 44% [2], though it seems that this figure has decreased somewhat coinciding with the introduction of continuous-flow pump devices [3–6]. As RVF has been shown to adversely affect patient outcomes after LVAD implantation [4, 5, 7], its relatively high incidence makes it a key issue for candidate selection and postoperative management in LVAD therapy.

The physiology of LVAD-related RVF is not well elucidated. Early studies suggested that increasing left ventricular output could precipitate RVF by way of two mechanisms: volume overloading of the right side of the heart owing to an increased flow in the systemic circulation or a decrease in right ventricular (RV) pump function caused by a septal shift into the left ventricle in the event of exaggerated drainage [8, 9]. These considerations have major implications for per- and postoperative management including pump settings and volume control relative to other factors such as pre-existing but unrecognized right myocardial dysfunction. However, the importance of these factors in the pathogenesis of LVAD-related RVF is unknown. A number of studies have addressed the preoperative evaluation of LVAD recipients and their risk of subsequent RVF development [2, 4, 5, 7, 10–12], but there is a paucity of studies describing haemodynamics in the days following LVAD implantation—the span of time during which RVF develops or becomes manifest. We hypothesized that information on the relative importance of early postimplantation haemodynamics and pump settings in LVAD patients in relation to

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the occurrence of RVF could help reveal findings that should prompt vigilance or even intervention from the attending physician following LVAD implantation.

Thus, the purpose of the present study was to compare haemodynamic responses and management in the early (72 h) postoperative period in patients who developed LVAD-related RVF with those who did not.

## METHODS

### Subjects

We performed a single-centre observational study of consecutive placement of HeartMate II devices (HMII, Thoratec, Pleasanton, CA, USA) in the Department of Cardiothoracic Surgery at Rigshospitalet, Copenhagen, Denmark. Since postoperative haemodynamic measurements were extracted from the current patient monitoring system, IntelliVue Clinical Information Portfolio (ICIP) (Philips Healthcare, Eindhoven, Netherlands) of the intensive care unit (ICU), only patients receiving a HMII after ICIP was implemented (July 2007 onwards) were considered for inclusion in the analysis. The inclusion was retrospective and ended in May 2012. The data registration was approved by the Danish Data Protection Agency (journal no. 2007-58-0015/30-0760).

### Data collection

All patient files were reviewed for information on preoperative patient characteristics, clinical status and biochemistry and for right heart catheterization data. Echocardiographic measurements were extracted from the hospital's echocardiography image management system (Xcelera R3.1L1, Philips Healthcare, Eindhoven, Netherlands).

Postoperative variables of interest were extracted from ICIP in the following way: for HMII readings, the values at the time of ICU arrival ($T_0$) and every hour up to 12 h postarrival ($T_{12}$) and then at $T_{24}$, $T_{48}$ and $T_{72}$ were recovered, validated and entered into an electronic database. Haemodynamic measurements, cardio-/vasoactive agent dosage, blood gas measurements and data concerning respiratory and renal function were recovered for times $T_0$, $T_4$, $T_8$, $T_{12}$, $T_{24}$, $T_{48}$ and $T_{72}$. In case of missing values, the measurement closest to the one missing but no more than 6 h remote was used. If no measurements were available within 6 h before or after the time in question, the value was recorded as missing.

Biochemical data from blood samples on days 1, 2 and 3 postimplantation (one set per day) were collected from patient files.

Thirty-day and 1-year post-implantation survival status was determined from the patient records. This approach was considered reliable as all recipients were affiliated to our hospital's cardiology department as out-patients with regular visits. The follow-up was complete for all patients.

RVF was defined as need for intravenous inotropic or vasodilator therapy >14 days postimplantation, nitric oxide (NO) therapy ≥48 h or RVAD therapy [2, 5]. The following cardio-/vasoactive agents were counted as inotropic or vasodilator therapy: dopamine, dobutamine, norepinephrine, epinephrine, milrinone, levosimendan and nitroglycerine. Nitroprusside is rarely used in Denmark. Due to the long half-life of levosimendan metabolites, we considered the duration of levosimendan treatment to be 1 week after cessation of the infusion.

### Recorded variables

The preoperative variables recorded were as follows: patient characteristics (height, weight, gender, age, aetiology of heart failure and preimplantation clinical status), echocardiographic data (right ventricular diameter (RVD) and tricuspid annular plane systolic excursion (TAPSE)), right heart catheterization data (central venous/right atrial pressure (CVP/RAP), mean pulmonary arterial pressure (MPAP), pulmonary capillary wedge pressure (PCWP), cardiac index (CI) and right ventricular stroke work index (RVSWI)), blood laboratory values (platelet count (PLT), white blood cell count (WBC), C-reactive protein (CRP), creatinine (CREA), blood urea nitrogen (BUN), alkaline phosphatase (ALP) and alanine transaminase (ALAT)).

The postoperative variables recorded were haemodynamic data (heart rate (HR), CVP, systolic, mean and diastolic pulmonary arterial pressure, left atrial pressure (LAP), mean arterial pressure (MAP), CI), HMII readings (pump flow, pump speed and motor power), cardio-/vasoactive therapy (dosage of dopamine, dobutamine, norepinephrine, epinephrine, milrinone, levosimendan and nitroglycerine), right heart failure alleviating therapy (NO, epoprostenol, sildenafil), blood gas analysis (arterial oxygen saturation, mixed or central venous oxygen saturation ($SvO_2$/$ScO_2$, respectively), arterial oxygen and carbondioxide partial pressure, mixed or central venous oxygen partial pressure, pH, lactate and haemoglobin concentrations), respiratory status (spontaneous or mechanical ventilation, ventilator mode and inhaled oxygen fraction), renal status (hourly urine output, cumulative urine output, whether or not on renal replacement therapy) and biochemical data (WBC, CRP, CREA, BUN, ALP and ALAT).

### Cardiac output measurement technique

All patients had a pulmonary artery catheter inserted before or during surgery. Cardiac output was measured at the attending clinicians' discretion using bolus thermodilution with room temperature saline according to the standard of the department.

### Data analysis

To facilitate comparison of cardio-/vasoactive therapy between patients, doses of the four catecholamine agents (dopamine, dobutamine, norepinephrine and epinephrine) in each patient were added into a single aggregate dose, considering equal volumes equivalent in terms of effect. This approach reflected the department's standard of preparing catecholamine suspensions according to patient weight so that 1 ml/h equals 1 μg/kg/min of dopamine and dobutamine and 0.01 μg/kg/min of epinephrine and norepinephrine. The aggregate catecholamine dose thus attained (total ml/h) was used for inter-patient comparisons. Comparable effects of dopamine, norepinephrine and epinephrine on systemic blood pressure have previously been demonstrated with a proportional dosage of dopamine 100 times that of norepinephrine and epinephrine [13].

A lactate level of ≥2.5 mM and a CVP of ≥15 mmHg were regarded as clinical markers of significant circulatory insufficiency and RV insufficiency, respectively [14, 15]. As several measurements of both variables were available for all patients, the proportions of measurements exceeding these thresholds were compared between the RVF and non-RVF groups. These

proportions were regarded as a rough estimate of the prevalence of haemodynamic impairment in each group over the 72 h studied.

All statistical analyses and graph designs were carried out with the SigmaPlot software package (Systat Software, Inc., Chicago, IL, USA). Between-group comparisons on normally distributed, continuous data were performed using Student's *t*-test. Mann–Whitney's *U*-test was used for comparison of categorical data and data that failed to meet the normality assumption (Shapiro–Wilk's test) or the equal variance tests. Within-patient variations over repeated measures were evaluated with the paired *t*-test (for two measures) or repeated measures analysis of variance (ANOVA) (for multiple measures). Proportions were compared with Fisher's exact test or, for sample sizes > 100, the $\chi^2$ test using Yate's continuity correction. The performance of CI at $T_0$ as a predictor of subsequent RVF diagnosis was tested by constructing a receiver operating characteristic (ROC) curve with pretest probability set at 0.3. The cut-off point was arbitrarily determined from the tabulated SigmaPlot report as the CI value at the inflection point of the positive and negative predictive values.

## RESULTS

Thirty-seven patients were considered for inclusion. Of these, 4 patients were not included as they were treated with another assist device at the time of HMII implantation. Of the remaining 33 patients, 11 patients met the criteria for RVF: 6 patients due to inotropic/vasodilator therapy, 4 patients due to NO therapy and 1 patient due to RVAD implantation. The RVAD was implanted concurrently with the LVAD owing to severe intraoperative right heart failure; thus, this patient contributed only to the analysis of preimplantation data. One patient died 33 h postimplantation while receiving large doses of both cardio-/vasoactive agents and NO, for which reason allocation to the RVF group (according to NO criterion) was considered most reasonable.

Patient characteristics and preoperative findings are presented in Table 1. Patients who subsequently developed RVF had poorer renal function as assessed by CREA and BUN than did non-RVF patients. RVF patients also tended to have lower PLT counts and be of higher age. Preoperative echocardiographic and right heart catheterization data were similar in the two groups.



**Table 1:** Baseline characteristics of the study participants

| Parameter | RVF (*n* = 11) | Non-RVF (*n* = 22) | *P*-value |
|---|---|---|---|
| Demography | | | |
| Age (years) | 62 (38–66) | 49.5 (29–60) | 0.113 |
| Gender distribution | | | |
| Male | 10 (91%) | 19 (86%) | 1.000 |
| Female | 1 (9%) | 3 (14%) | |
| Height (cm) | 181.4 ± 8 | 181.6 ± 6.6 | 0.931 |
| Weight (kg) | 83.7 ± 16.1 | 86.4 ± 15.1 | 0.639 |
| BSA ($m^2$) | 2.04 ± 0.21 | 2.07 ± 0.19 | 0.788 |
| Ischaemic heart disease | 3 (27%) | 7 (32%) | 1.000 |
| Biochemistry | | | |
| PLT ($10^9$/l) | 173 (149–266) | 236 (211–288) | 0.056 |
| WBC ($10^9$/l) | 8.4 (6–14.1) | 9.5 (7.2–10.1) | 0.909 |
| CRP (mg/l, median) | 19 (12–40) | 14 (7–52) | 0.553 |
| CREA (μM) | 178 ± 48 | 101 ± 41 | <0.001 |
| BUN (mg/l) | 42.3 (32.8–86.6) | 24.6 (17.1–45.9) | 0.025 |
| ALP (U/l) | 110 (69–158) | 97.5 (51–163) | 0.557 |
| ALAT (U/l) | 38 (22–196) | 40 (24–169) | 0.983 |
| Echocardiography | | | |
| TAPSE (cm) | 1.7 (1.4–2.3) | 1.5 (1.3–1.9) | 0.317 |
| RVD (cm) | 4.1 ± 0.4 | 4.1 ± 0.8 | 0.280 |
| Right heart catheterization | | | |
| CVP/RAP (mmHg) | 13.8 ± 4.6 | 13.2 ± 3.5 | 0.686 |
| MPAP (mmHg) | 35.5 ± 5 | 38.9 ± 7.4 | 0.200 |
| PCWP (mmHg) | 27 (24–28) | 28(25–29.5) | 0.595 |
| CI (l/min/$m^2$) | 1.95 (1.7–2.3) | 1.9(1.6–2.5) | 0.848 |
| SVI (ml/$m^2$) | 23.2 ± 6.5 | 21.4 ± 6.1 | 0.471 |
| RVSWI (g m/$m^2$) | 6.8 ± 2.2 | 7.7 ± 3.2 | 0.423 |
| CVP/PCWP ratio | 0.48 (0.39–0.63) | 0.5 (0.4–0.59) | 0.175 |
| Clinical status | | | |
| Ventilator therapy | 0 | 0 | – |
| I.v. cardio-/vasoactive therapy | 6 (55%) | 14 (64%) | 0.714 |
| Number of i.v. cardio-/vasoactive agents | 1 (0–2) | 1 (0–2) | 0.888 |

Continuous data are presented as mean ± standard deviation or median (inter-quartile range); categorical data are presented as number (%).
ALAT: alanine aminotransferase; ALP: alkaline phosphatase; BSA: body surface area; BUN: blood urea nitrogen; CI: cardiac index; CREA: creatinine; CRP: C-reactive protein; CVP: central venous pressure; i.v.: intravenous; MPAP: mean pulmonary arterial pressure; PCWP: pulmonary capillary wedge pressure; PLT: platelet count; RAP: right atrial pressure; RVD: right ventricular diameter; RVF: right ventricular failure; RVSWI: right ventricular stroke work index; SVI: stroke volume index; TAPSE: tricuspid annular plane systolic excursion; WBC: white blood cell count.

**Table 2:** Change in right heart catheterization values from the preoperative examination to the arrival in the ICU

| Parameter | RVF | Non-RVF | *P*-value |
|---|---|---|---|
| CVP/RAP (mmHg) | −1.3 ± 6 | −3 ± 3.8* | 0.39 |
| MPAP (mmHg) | −12.6 ± 8.8* | −11 ± 6.5** | 0.58 |
| PCWP/LAP (mmHg) | −17.6 ± 5.2* | −15.2 ± 6.5** | 0.44 |
| CI (l/min/m$^2$) | 0.2 ± 0.5 | 0.96 ± 0.8** | 0.018 |
| RVSWI (g m/m$^2$) | −4.3 ± 2.0** | −0.9 ± 2.0 | <0.001 |

Values are presented as mean ± standard deviation. *$P$ < 0.01 and **$P$ < 0.001.
HMII: Heartmate II; RVF: right ventricular failure; CVP: central venous pressure; RAP: right atrial pressure; MPAP: mean pulmonary arterial pressure; PCWP: pulmonary capillary wedge pressure; LAP: left atrial pressure; CI: cardiac index; RVF: right ventricular failure; RVSWI: right ventricular stroke work index.

Crude survival rates were 87.9% on day 30 and 72.7% at 1 year/transplantation. According to group, survival rates were 63.6% for RVF vs 100% for non-RVF patients on day 30 ($P$ = 0.008) and 45.5 vs 86.4% at 1 year/transplantation ($P$ = 0.033).

## Immediate postoperative findings

The impact of HMII implantation on right heart catheterization variables is given in Table 2. Whereas CVP and MPAP decreased to a similar degree in both groups, there was a significant difference in the CI response to HMII implantation. In the RVF group, the constant CI in the face of a marked reduction in MPAP reflected a significant RVSWI decrease, whereas in the non-RVF group, the MPAP reduction was matched by a corresponding CI increase to yield an unaltered RVSWI.

CI values in the two groups before and after HMII implantation are depicted in Fig. 1.

## Haemodynamic changes from $T_0$ to $T_{72}$

In Table 3, haemodynamic indices and cardio-/vasoactive treatment characteristics of the two groups at $T_0$ and $T_{72}$ are presented (intermediate values were omitted from the table for the sake of clearness). Notably, the significantly higher CI and RVSWI values in the non-RVF group at $T_0$ were present in spite of a significantly lower aggregate dose of catecholamines. Although the differences in CI and RVSWI had evened out at $T_{72}$, during this time milrinone dosage had become significantly higher in the RVF group when compared with the non-RVF group and the difference in aggregate catecholamine dose had increased even further.

Figure 2 depicts the development over time of CI, MAP, CVP and P-lactate in both groups in detail.

For the haemodynamic indices included in Table 2, two-way repeated measures (RM)-ANOVA including all measurement times in the data set was performed. For the variables CI and MAP, significant interaction between the factors group and time was found, confirming that the development of the two variables over time differed significantly between the two groups.

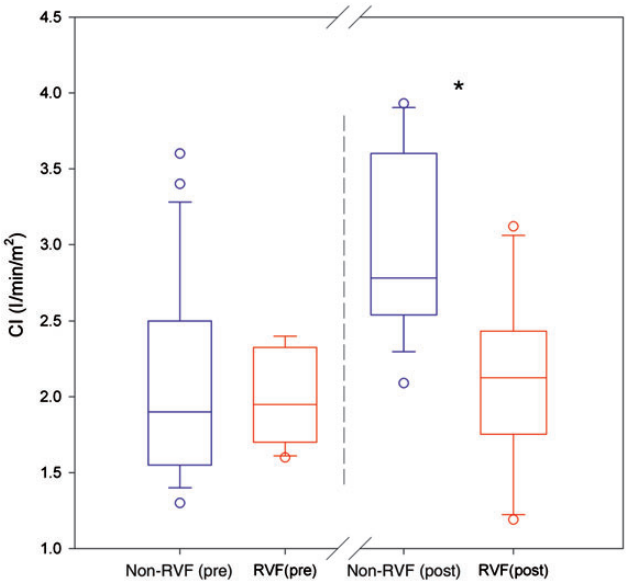


**Figure 1:** Box-and-whisker plot of CI before and immediately after LVAD implantation according to group. Pre: value at preoperative right heart catheterization; RVF: right ventricular failure; post: value at arrival in ICU. *$P$ < 0.001 between groups after LVAD implantation.

## Discriminative analyses

As CI values at $T_0$ differed significantly between the two groups, we performed a ROC analysis to test the predictive value of low CI at $T_0$ for subsequently fulfilling the criteria for RVF. At a cut-off value of 2.3 l/min/m$^2$, the test yielded a sensitivity of 70%, a specificity of 94% and positive and negative predictive values of 84 and 88%, respectively (Fig. 3). ROC area was 0.894 (confidence interval 0.764–1, $P$ < 0.001) (Fig. 4).

As for lactate and CVP measurements, the proportion of lactate measurements ≥2.5 mM was 57.3% in the RVF group and 19.7% in the non-RVF group ($P$ < 0.001). The figures for CVP measurements ≥15 mmHg were 53.1 and 18.3%, respectively ($P$ < 0.001).

# DISCUSSION

Our findings indicate that RVF following HMII implantation—a condition that by most definitions, including the current one, requires clinical criteria to be present as late as 14 days postimplantation—is manifest already in the immediate postoperative period, as shown by the considerable difference in CI and RVSWI at $T_0$ between RVF and non-RVF patients. Although CI in RVF patients approached that of the non-RVF patients over the 72 h studied, this seemed to be a consequence of extended cardio-/vasoactive therapy rather than of a restitution of RV performance. Both crude mortality and the prevalence of circulatory dysfunction as assessed by lactate and CVP measurements were significantly higher in the RVF group, confirming that the complication entails serious adverse effects on patient condition and prognosis.

## Preoperative and immediate postoperative findings

In agreement with some of the other studies, we found that poorer renal function [4, 10] and low PLT counts [2, 10] (the latter, however,

**Table 3:** Haemodynamic indices and cardio-/vasoactive drug therapy at the time of arrival in the ICU ($T_0$) and after 72 h ($T_{72}$) in the RVF and non-RVF groups

| | $T_0$ | | | $T_{72}$ | | | |
|---|---|---|---|---|---|---|---|
| | RVF | Non-RVF | *P*-value | RVF | Non-RVF | *P*-value | |
| Haemodynamic indices | | | | | | | RM-ANOVA |
| HR (bpm) | 109 ± 24 | 108 ± 14 | 0.855 | 97 ± 14 | 104 ± 16 | 0.281 | *N* |
| CVP/RAP (mmHg) | 13.3 ± 4.6 | 10.0 ± 3.1 | 0.037 | 16.4 ± 4.1 | 13.2 ± 4.1 | 0.087 | *T* |
| MPAP (mmHg) | 23.4 ± 5.6 | 27.8 ± 6.2 | 0.066 | 28.6 ± 4.4 | 31.2 ± 4.7 | 0.245 | – |
| LAP (mmHg) | 11.3 ± 2.7 | 11.5 ± 4.6 | 0.953 | N/A | N/A | | – |
| MAP (mmHg) | 62 ± 15 | 72 ± 11 | 0.045 | 67 ± 11 | 83 ± 11 | 0.001 | *I* |
| CI (L/min/m$^2$) | 2.1 ± 0.5 | 3.0 ± 0.6 | <0.001 | 2.4 (2.1–3.3) | 2.8 (2.6–3.2) | 0.334 | *I* |
| RVSWI (g m/m$^2$) | 3.3 (2.5–3.8) | 6.4 (4.6–8.5) | <0.001 | 4.8 (2.9–6.1) | 5.8 (4.5–6.7) | 0.232 | *N* |
| $SvO_2$ (%) | 63.1 ± 10.8 | 67.2 ± 8.4 | 0.254 | 56.6 ± 11 | 60 ± 7.7 | 0.398 | *T* |
| Lactate (mM) | 3.2 (1.7–7.2) | 1.8 (1.1–2.3) | 0.048 | 1.5 (1.2–2.0) | 1.3 (1.0–1.4) | 0.314 | *T* |
| Pump speed (rpm) | 9566 ± 531 | 9819 ± 496 | 0.216 | 9680 ± 569 | 9855 ± 390 | 0.349[b] | – |
| Pump flow (L/min) | 4.9 ± 0.9 | 5.6 ± 0.9 | 0.027 | 5.5 ± 1.2[g] | 5.7 ± 1.2[g] | 0.508 | – |
| Cardio-/vasoactive therapy | | | | | | | *P*-value, $\Delta T_0$–$T_{72}$ |
| Total catecholamine dose (m/h) | 14.0 (8.8–23.8) | 6.5 (4–12.3) | 0.034 | 16.0 (9–23.5) | 0 (0–2.5) | <0.001 | 0.011 |
| Milrinone dose (μg/kg/min) | 0.25 (0.13–0.38) | 0.23 (0.01–0.36) | 0.450 | 0.37 (0.10–0.44) | 0 (0–0.30) | 0.026 | 0.221 |
| Nitroglycerine dose (μg/kg/min) | 0 (0–0.28) | 0.20 (0.01–0.42) | 0.082 | 0 (0–0) | 0 (0–0.26) | 0.327 | 0.391 |

Two-way RM ANOVA using time and group as factors was carried out for all haemodynamic indices. For catecholamine, milrinone and nitroglycerine dosage, within-patient changes from $T_0$ to $T_{72}$ only were compared between groups. No patients received levosimendan during the period studied. Continuous data are presented as mean ± standard deviation or median (inter-quartile range); categorical data are presented as number (%).
Bpm: beats per minute; CI: cardiac index; CVP: central venous pressure; HR: heart rate; LAP: left atrial pressure; MAP: mean arterial pressure; MPAP: mean pulmonary arterial pressure; RAP: right atrial pressure; rpm: rotations per minute; RVF: right ventricular failure; RVSWI: right ventricular stroke work index; $SvO_2$: mixed venous oxygen saturation; $\Delta T_0$–$T_{72}$: change from $T_0$ to $T_{72}$. *T*: significant effect of the factor time ($P < 0.05$); *I*: significant interaction between the factors group and time ($P < 0.05$); *N*: no significant effects; N/A: values not available due to abundance of missing data; –: analysis not performed due to frequent missing values or non-normality of data.



only bordering statistical significance) preoperatively were associated with post-LVAD implantation RVF. Right heart catheterization and echocardiographic findings did not discriminate patients who did and those who did not develop RVF in this study. With respect to the catheterization data, this is in line with the findings of some [2, 5, 7, 11]—but in contrast to other [4, 10, 12]—previous studies. Our echocardiographic findings are difficult to compare with the other studies cited in this article as these did not report on RVD and TAPSE; significant differences have been reported in preoperative left ventricular end-systolic and -diastolic diameter [2], tricuspid regurgitation severity score [5] and presence of severe RV systolic dysfunction (unspecified method of estimation) [10].

The pronounced difference in the effect of HMII implantation on RV performance as assessed by CI and RVSWI already in the immediate postoperative phase seems to indicate that occult RV impairment was present already pre- or intraoperatively. The severely decreased left ventricular function that prompted LVAD treatment might thus have concealed large differences among referred patients in right heart performance, differences that were unmasked with the augmentation of the systemic circulation provided by the LVAD and possibly by unspecific intraoperative RV injury. Notably, the upholding at $T_0$ of a CI similar to the preoperative value in the RVF group required significantly larger doses of inotropic support than did the marked increase in the non-RVF group.

## Postoperative haemodynamic observations

Although CI in RVF patients increased to the same level as that of non-RVF patients during the 72 h studied, this only happened in the face of an increasing difference in the intensity of cardio-/vasoactive therapy; thus, while the majority of non-RVF patients had been weaned from catecholaminergic agents by $T_{72}$, the aggregate dosage of these agents was virtually similar at $T_0$ and $T_{72}$ in the RVF group. Furthermore, the MAP increase in the non-RVF group towards $T_{72}$ in the face of an unaltered CI indicates a normalization of peripheral vascular function that did not take place in the RVF group. The reason for this is unclear but could in part be due to the non-RVF patients being weaned from nitroglycerine and milrinone, or conversely, it could be interpreted as overzealous use of inodilators or nitroglycerine in the RVF group.

Though only indirect markers of RV and circulatory dysfunction, the higher prevalence of elevated CVP and lactate levels in the RVF group underscores the effects of cardiac dysfunction, revealing itself in both backward failure and inadequate target organ perfusion.

## Right ventricular failure after left ventricular assist device implantation

Owing to the structural complexity of ventricular interdependence, the pathophysiology of LVAD-related RVF is not easily understood and may well be multifactorial.

Viewed in its conceptually simplest form, the relation between the two ventricles is that of two pumps mutually connected in series into a closed circuit. Considered in this way, the cause of LVAD-related RVF may be the simple unmasking of a pre-existing RV dysfunction with the augmentation of systemic circulatory function; indeed, the increased LV output could contribute to a pre-existing RV dysfunction by causing a volume overload of the RV [16].

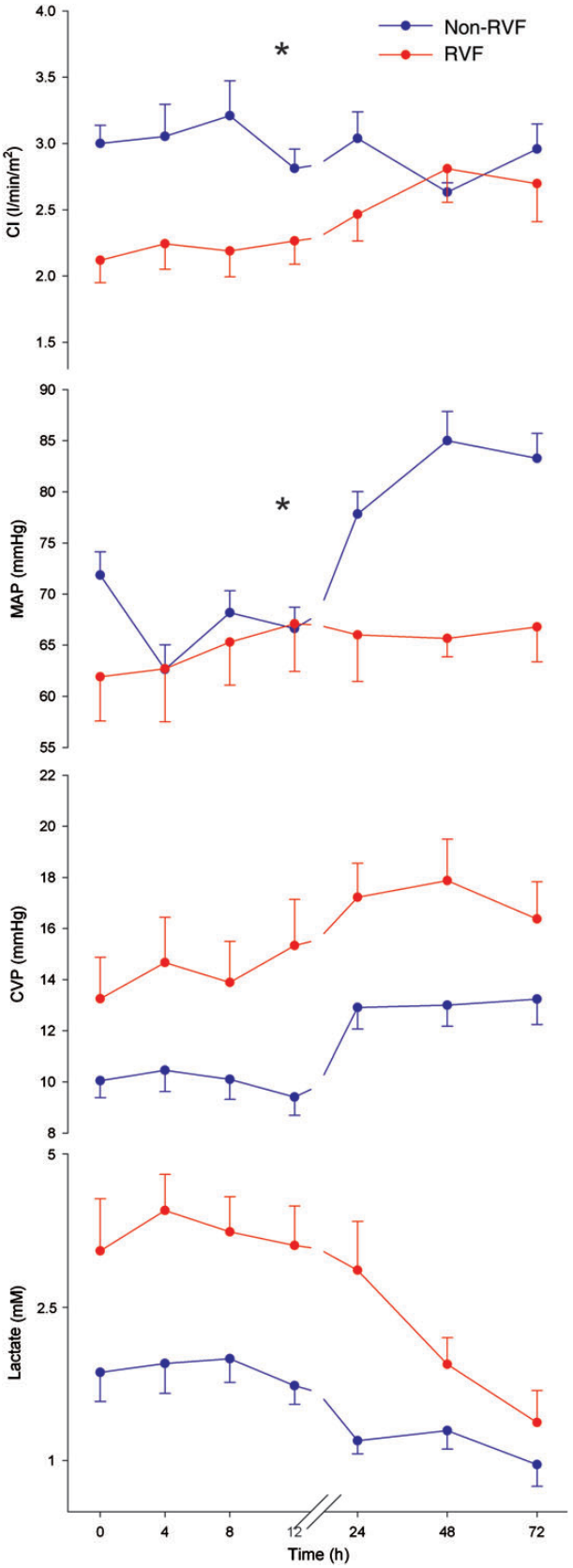


**Figure 2:** Course of development for haemodynamic indices from arrival in the ICU ($T_0$) until 72 h postimplantation ($T_{72}$). Graphs marked with an asterisk depict parameters that exhibited significant interaction between the factors group (RVF/non-RVF) and time in repeated measures ANOVA. Lactate concentration values were log-transformed to obtain a normal distribution; accordingly, the scaling of the ordinate in the bottom (lactate) graph is logarithmic. Error bars are standard error of the mean. CI: cardiac index; CVP: central venous pressure; MAP: mean arterial pressure; RVF: right ventricular failure.

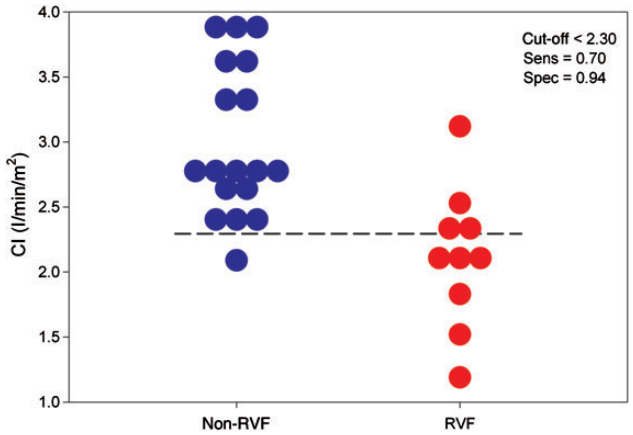


**Figure 3:** Histogram of CI at the time of arrival in the ICU ($T_0$) in each group. RVF: right ventricular failure; Sens: sensitivity; Spec: specificity.

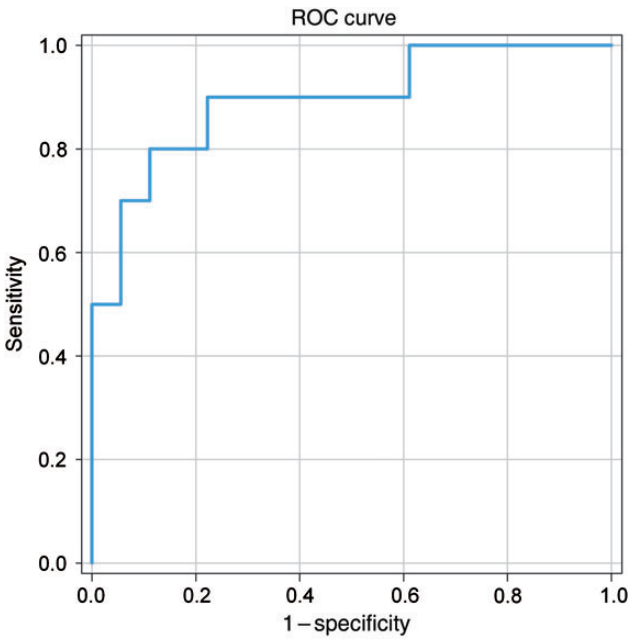


**Figure 4:** ROC curve of CI at $T_0$ as a predictor of subsequent RVF diagnosis.

However, in addition to being coupled in series, the two ventricles exhibit a mechanical interdependence owing to their anatomical position; in particular, the thin-walled RV is dependent on the function of the interventricular septum (IVS) for the maintenance of an adequate pump output [17]. Thus, emptying of the LV by exaggerated LVAD pump flow could interfere with RV function by compromising the vital contribution of the IVS to RV contraction [1]. This has prompted some investigators to caution against high pump settings immediately after LVAD implantation [15]. On the other hand, the reduction in left ventricular congestion obtained by appropriate draining may relieve the RV by reducing

RV afterload, increasing aortic and thus coronary blood flow and reversing a septal shift into the right ventricle from a distended left ventricle.

The results of our study do not demonstrate an obvious association between high pump speed and subsequent RVF development as pump speed was similar in the two groups. Pump speed was not set to a fixed value in the operating theatre but rather adjusted peri and postoperatively according to the haemodynamic situation as assessed by transoesophageal echocardiography as well as PCWP and CI. Hence, we cannot exclude that if pump speed had been set lower in patients with low CI at $T_0$, fewer patients would have developed RVF. Future, preferably randomized studies involving intervention specifically on pump speed parameters are required to resolve this issue. However, the fact that the RVF group already at $T_0$ had a substantially lower CI than the non-RVF group while on similar pump speed settings makes it unlikely that the mechanism primarily responsible for RVF development should be one of gradual RV overfilling by exaggerated LVAD pumping.

### Study limitations

Our study has a number of limitations, including the small number of included patients and the single-centre design; thus, the risk factors identified may, to an unknown extent, reflect bias owing to local therapeutic practices or merely random statistical variation whereas other risk factors may have been missed due to lack of statistical power. Secondly, the limitations are enhanced by the study being retrospective as this compromises both the availability of data (i.e. missing values) and the reliability and accuracy of especially haemodynamic measurements. However, the finding of rather highly significant differences—even in a material as small as the present—suggests that the impact of such blurring was limited. Furthermore, the study population did show attributes comparable with the populations of previous studies as we confirmed earlier findings of between-group differences in PLT counts and renal function parameters [2, 4, 10].

## CONCLUSION

In our study, CI immediately after LVAD surgery predicted development of RVF 2 weeks postoperatively according to a standard definition. Overall, the results of the present study suggest that the sequence of pathophysiological events leading to LVAD-related RVF begins during or immediately after device implantation. This temporal course indicates that the condition in most cases is either present in a subclinical form already preoperatively or arises intraoperatively rather than as a result of the postoperative management. Taking the small sample size into account, care should be taken in generalizing the results; however, the study may serve as a hypothesis-generating tool for future research.

**Conflict of interest:** Finn Gustafsson is a member of the Thoratec Advisory Board.

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