Association of Inflow Cannula Position with Left Ventricular Unloading and Clinical Outcomes in Patients with HeartMate II Left Ventricular Assist Device

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The relationship between the HeartMate II left ventricular assist device (LVAD) position and pump thrombosis has been reported. However, further clinical implications of device position are unknown. This study aimed to investigate optimal device position for better left ventricular (LV) unloading and patient prognosis. Patients undergoing a ramp test with right heart catheterization after HeartMate II LVAD implantation were enrolled to this study. Device position was quantified from the chest X-ray obtained at the time of the ramp test: (1) inflow cannula angle relative to horizontal line, (2) pump angle relative to spine, (3) pump depth, (4) angle between inflow cannula and pump, and (5) angle between pump and outflow graft. LV unloading was assessed by pulmonary capillary wedge pressure at set LVAD speed. Fifty-four patients (60 years old and 34 male [63%]) were enrolled. Nobody experienced device malfunction during the study period. Increased LV unloading (*i.e.*, lower pulmonary capillary wedge pressure) was associated with a narrower inflow cannula angle relative to horizontal line. Inflow cannula angle <75° was associated with higher 1 year heart failure readmission-free survival rate ($p < 0.05$, hazards ratio 7.56 [95% confidence interval 2.32–24.7]). In conclusion, HeartMate II LVAD inflow cannula position was associated with LV unloading and patient prognosis. Prospective studies to ensure optimal device positioning and target better clinical outcomes are warranted. *ASAIO Journal* 2019; 65:331–335.

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Left ventricular assist device (LVAD) therapy is a widely used treatment for advanced heart failure (HF) patients both as a bridge to transplantation or as a destination therapy.[1,2] Despite this, device implantation techniques have not been standardized, and clinical outcomes vary by institution.[3] Device position (*i.e.*, inflow cannula, pump, and outflow graft positions) has been identified as a risk factor for pump thrombosis.[4–6] For example, a narrow angle between inflow cannula and pump and a shallow pump pocket, as assessed by chest X-ray (CXR), were associated with the development of pump thrombosis.[6] In the The PREVENtion of HeartMate II pump Thrombosis through clinical management (PREVENT) trial, adequate surgical technique including positioning the inflow cannula parallel to the septum and fixating the pump to prevent migration, in addition to other management strategies, was associated with a reduced pump thrombosis rate.[3] Furthermore, a malpositioned inflow cannula may contact the endocardium and lead to refractory ventricular tachyarrhythmia.[7] Accordingly, unification of implantation techniques for optimal device positioning has been proposed.[8]

However, the clinical implications of device position, other than pump thrombosis, are not well understood. Device positioning may affect left ventricular (LV) unloading, with insufficient unloading, leading to HF readmissions, decreased quality of life, and worse long-term outcomes. We recently demonstrated in HVAD (Medtronic, Minneapolis, MN) patients that a lower horizontal angle of the inflow cannula was associated with better LV unloading.[9] However, the relationship between HeartMate II pump position and LV unloading has not been previously reported. In this study, we investigated the association between HeartMate II LVAD position (cannula and pump) and LV unloading, as well as patient prognosis.

METHODS

Patient Selection

Consecutive clinically stable outpatients who prospectively underwent an echocardiographic and hemodynamic ramp test after HeartMate II LVAD implantation between April 2014 and August 2016 were enrolled into this analysis. Patients with suspected pump thrombosis were excluded from the study. A postero-anterior CXR obtained at time of ramp test was reviewed. LVAD implantation was performed by two experienced attending surgeons according to recommended surgical procedure. The inflow cannula was oriented parallel to the septum, and

the pump was placed below the diaphragm, with the outflow graft placed to the right of the sternum. The study protocol was approved by the institutional review board, and written informed consent was obtained from all patients before this study.

Ramp Test Protocol

Details of the ramp test protocol were reported previously.[10] The test was performed in the cardiac catheterization laboratory using transthoracic echocardiography and right heart catheterization as part of routine clinical care. LVAD speed was reduced to 8000 rpm, and echocardiographic and hemodynamic data were obtained. The speed was then increased in 400 rpm increments up to a speed of 12,000 rpm. Repeat echocardiographic and hemodynamic data were obtained in each speed. At the end of the test, the attending cardiologist reviewed the results and determined the appropriate LVAD set speed targeting a pulmonary capillary wedge pressure (PCWP) <18 mm Hg, central venous pressure <12 mm Hg, and cardiac index >2.2 L/min/m^2.[11] The degrees of mitral valve regurgitation were grade as follows: 0, none; 1, trace; 2, mild; 3, moderate; 4, moderate to severe; 5, severe. After the test, participants were followed at the set speed.

Radiographic Assessments

Posterior–anterior CXRs were obtained around the time of the ramp test to measure device position parameters. All CXRs were reviewed by two blinded experts, and each measurement was averaged. Measurements taken for the study are summarized in **Figure 1**. All radiographs were obtained in standing position, and we confirmed that sternal wires were directly overlying the vertebra in all cases before the measurements.

The following measurements of pump position were made: 1) angle between inflow cannula and the horizontal line, 2) angle between pump body and the spine, 3) angle between inflow cannula and the pump body, and 4) angle between pump body and the outflow graft. Pump depth was measured from the dome of the right hemidiaphragm to the bottom of the pump body.

Other Variables Evaluated

Patient demographics and clinical data before LVAD implantation were obtained. During the ramp test, hemodynamic and echocardiographic data were obtained per protocol. LV unloading was assessed by the absolute value of PCWP at final set speed after the ramp test. All patients were followed at the LVAD speed set at the end of ramp test, and death or HF readmission was recorded during a 1-year study period after the ramp test. HF readmission was defined as hospitalization to treat volume overload with intravenous diuretics. All events were counted and adjudicated by two independent researchers.

Statistical Analyses

All statistical analyses were performed using SPSS Statistics 22 (SPSS Inc, Chicago, IL). Variables with $p < 0.05$ were considered significant. Continuous variables were expressed as median (25% quartile, 75% quartile) and compared using Mann–Whitney U test. Categorical variables were compared using Fisher exact test. Interobserver variability in device position parameters was assessed by Ebel's intraclass correlation coefficient.

Logistic regression analyses were used to assess the association of each device position parameter with adequate LV unloading, defined as PCWP <18 mm Hg at the set LVAD speed. Variables with $p < 0.05$ were transformed into dichotomous variables with cutoff value calculated by receiver operating characteristic (ROC) analyses.

The prognostic impact of device position parameters was analyzed by Cox proportional hazards ratio regression analysis for the end-point of death or HF readmission. Continuous variables with $p < 0.05$ were transformed into dichotomous variables by using ROC analyses. Patient prognosis was assessed by Kaplan–Meier analyses and compared by log-rank test.

RESULTS

Baseline Characteristics

Fifty-four HeartMate II LVAD patients (60 years old and 34 male) were enrolled. Most of the patients received LVAD implantation as destination therapy (85%), and 26 (49%) had an ischemic etiology for their HF (**Table 1**). Patients underwent ramp test at 324 days after LVAD implantation. Echocardiographic and hemodynamic data during ramp test were summarized in **Table 1**.

Device Position Parameters

Inter-rater reliabilities of device parameters were 0.995 for inflow cannula angle, 0.997 for pump angle, 0.992 for

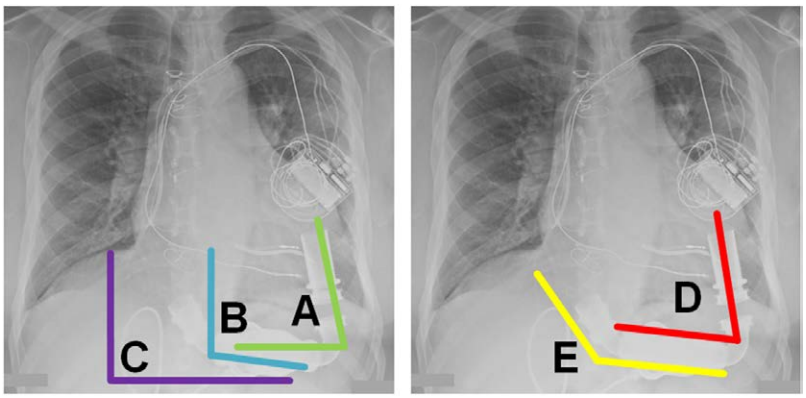

Figure 1. Device position parameters measured. A, Inflow cannula angle; B, pump angle relative to spine; C, pump depth; D, angle between inflow cannula and pump; and E, angle between pump and outflow graft. full color online

Table 1. Clinical Variables Obtained at Ramp Tests

	N = 54
Days between LVAD implantation and ramp test	324 (124, 862)
Demographics	
Age (y)	60 (54, 70)
Body mass index	31.0 (25.7, 36.3)
Male	34 (63%)
Destination therapy	45 (83%)
Ischemic etiology	26 (48%)
Hypertension	33 (61%)
Diabetes mellitus	21 (39%)
Atrial fibrillation	16 (30%)
History of ventricular tachyarrhythmia	10 (19%)
Chronic obstructive pulmonary disease	11 (20%)
Device position parameters	
Inflow cannula angle (degrees)	68 (62, 79)
Pump angle relative to spine (degrees)	95 (82, 103)
Pump depth (mm)	104 (85, 126)
Inflow cannula–pump angle (degrees)	67 (61, 73)
Pump-outflow graft angle (degrees)	115 (108, 125)
Variables at set LVAD speed	
LVAD speed (rpm)	9,400 (9,000, 9,600)
LVDd (cm)	5.8 (5.1, 7.0)
Opening of aortic valve	19 (35%)
Mitral valve regurgitation (degrees)	0 (0, 1)
CVP (mm Hg)	8 (5, 12)
Mean PAP (mm Hg)	25 (20, 31)
PCWP (mm Hg)	13 (8, 16)
CI (L/min/m^2)	2.56 (2.29, 3.00)

CI, cardiac index; CVP, central venous pressure; LVDd, left ventricular diastolic diameter; PAP, pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure.

pump depth, 0.989 for angle between inflow cannula and pump, and 0.987 for angle between pump and outflow graft. Distributions of device position parameters are shown in **Figure 2**.

The median inflow cannula angle relative to the horizontal line was 68° (62°, 79°). Minimal angle was 40°, and 5 patients had the angle above 90° (*i.e.*, cannula was directed towards lateral wall). The median angle between inflow cannula and pump was 67° and ranged between 50° and 95°.

Device Position and LV Unloading at Set Speed

Median set speed was 9,400 (9,000, 9,600) rpm, and PCWP was 13 (8, 16) mm Hg. Among all device position parameters, an inflow cannula angle ≤75°, which was calculated by ROC analysis (see Figure 1A, Supplemental Digital Content, http://links.lww.com/ASAIO/A288), was the only significant predictor of sufficient LV unloading (defined as PCWP <18 mm Hg at set speed; **Table 2**; odds ratio 11.1, 95% confidential interval 2.09–59.0). The PCWP in patients with inflow cannula angle ≤75° was significantly lower than those with inflow cannula angle >75° (12° [8°, 15°] *vs.* 16° [10°, 20°], p =0.034; **Figure 3)**. Also, mean pulmonary artery pressure was lower, and cardiac index was higher in patients with angle ≤75° compared with those with angle >75° (see Table 1, Supplemental Digital Content, http://links.lww.com/ASAIO/A290).

Suction events during the ramp study were not common in our study population. Twelve tests were stopped early because of suction. The median inflow cannula angle in these patients was 68° (63°, 70°) as compared with 68° (62°, 83°) in the remaining patients (p = 0.57).

Device Position and Clinical Outcome

During the study period, 13 patients (24%) experienced death or HF admission (eight death and five HF admission). There were no cases of pump thrombosis after the ramp study. An inflow cannula angle >75°, which was calculated by ROC analysis (see Figure 1B, Supplemental Digital Content, http://links.lww.com/ASAIO/A289), was a significant predictor of death or HF admission in uni/multivariate Cox analyses (**Table 3**; hazards ratio 7.56, 95% confidential interval 2.32–24.7). Conversely, patients with an inflow cannula angle ≤75° had a higher HF admission-free survival rate compared with those with an angle >75° (**Figure 4**; 88.6% *vs.* 41.7%, p < 0.001). When the outcome components were assessed independently, survival was not affected by the inflow cannula angle (p = 0.56), but the rate of HF readmissions was significantly affected (p <0.001).

Patients with inflow cannula angle ≤75° were more likely to have an ischemic etiology and less likely to have a history

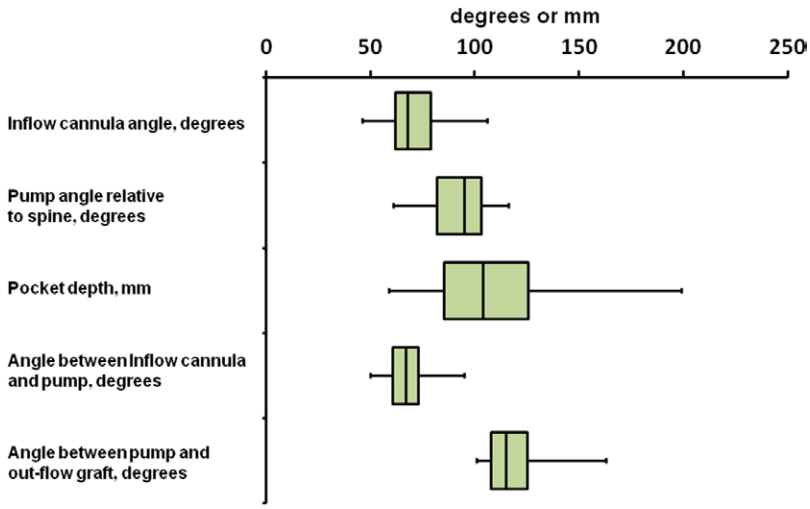

Figure 2. Distributions of device position parameters. full color online

Table 2. Logistic Regression Analyses for Left Ventricular Unloading at Set Speed

	P	Odds Ratio (95% CI)
Continuous variables		
Inflow cannula angle	0.008*	0.91 (0.86–0.98)
Pump angle relative to spine	0.13	0.95 (0.88–1.02)
Pocket depth	0.80	1.00 (0.98–1.03)
Inflow cannula–pump angle	0.091	0.94 (0.88–1.01)
Pump-outflow angle	0.14	0.97 (0.93–1.01)
Dichotomous variables		
Inflow cannula angle ≤75 degrees	0.005*	11.1 (2.09–59.0)

*$p < 0.05$ by logistic regression analyses.
CI, confidence interval.

Table 3. Cox Proportional Hazard Ratio Regression Analyses for the End-point of Death or HF Readmission

	P Value	Hazard Ratio (95% CI)
Continuous variables		
Inflow cannula angle	0.004*	1.05 (1.02–1.09)
Pump angle relative to spine	0.18	1.03 (0.99–1.08)
Pocket depth	0.15	0.98 (0.96–1.01)
Inflow cannula–pump angle	0.05	1.05 (1.00–1.09)
Pump-outflow angle	0.52	1.01 (0.98–1.05)
Dichotomous variables		
Inflow cannula angle >75 degrees	0.001*	7.56 (2.32–24.7)

*$p < 0.05$ by Cox proportional hazard ratio regression analysis.
CI, confidence interval.

of ventricular tachyarrhythmia (Table 1, Supplemental Digital Content, http://links.lww.com/ASAIO/A290). Comparisons of each position parameter stratified by the inflow cannula angle are shown in Table 1, Supplemental Digital Content, http://links.lww.com/ASAIO/A290, and there were no significant differences between two groups ($p > 0.05$ for all).

DISCUSSION

In this study, we analyzed the clinical implications of cannula and pump positions on LV unloading and patient prognosis during HeartMate II LVAD support. Our main finding is that narrower inflow cannula angle (≤75°), which was assessed by CXR at time of ramp test, was associated with LV unloading at set speed and higher HF admission-free survival rate, whereas other device position parameters did not affect these clinical outcomes This is the first report to demonstrate the impact of inflow cannula angle on LV unloading and HF occurrence during HeartMate II support.

Device Position and LV Unloading at Set Speed

LVAD aims to unload the LV and augments forward flow, alleviating HF symptoms and improving survival. The assessment of LV unloading can be achieved with imaging modalities or with direct measurement of LV pressure. In the current study, we assessed LV unloading by using PCWP as a surrogate marker for LV end-diastolic pressure. The size of the LV as assessed by two-dimensional echocardiography at the end of the diastolic period can also be a marker of the degree of LV unloading. Both the absolute values of LV end-diastolic diameter or PCWP and the change in those value in response to speed change are good assessments of LV unloading, but we believe that a lower PCWP at set speed is a true evidence of sufficient LV unloading.[12]

A narrower (more horizontal) inflow cannula angle was associated with better LV unloading. Specifically, we identified that a cannula position >75° (vertical or laterally directed) impaired sufficient pump function. Patients with extreme inflow cannula angulation (>90°) had the worst LV unloading, with a median PCWP of 20 (16, 25) mm Hg. This finding highlights the importance of maintaining an inflow cannula position that is directed at the mitral valve to promote better flow patterns and efficient LV unloading.

Device Position and Prognosis

A narrower inflow cannula angle (≤75°) was also associated with a reduction in adverse outcomes, particularly HF readmissions. This provides a clinical correlation to the physiological observation that vertical or laterally oriented cannulae do not unload, as well as appropriately oriented cannula.

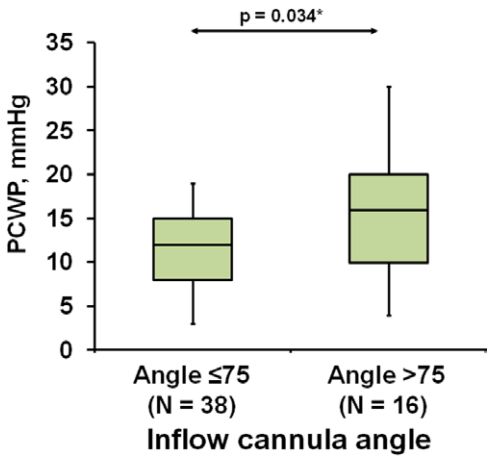

Figure 3. Pulmonary capillary wedge pressure (PCWP) stratified by the cutoff of inflow cannula angle (75°). *$p < 0.05$ by Mann–Whitney U test. full color online

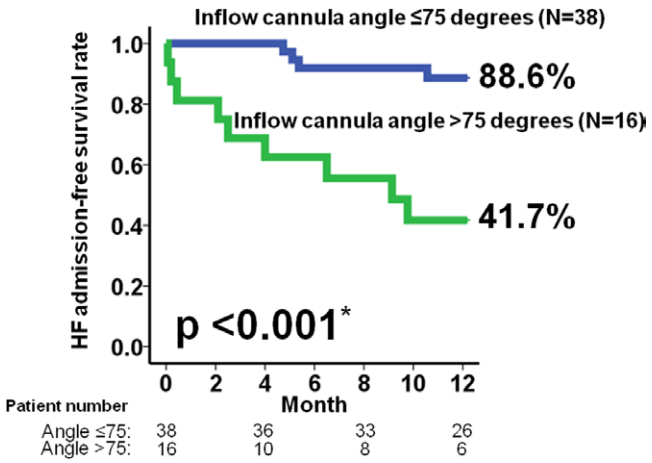

Figure 4. Heart failure (HF) readmission-free survival rate stratified by the cutoff of inflow cannula angle (75°). *$p < 0.05$ by log-rank test. full color online

Furthermore, inflow cannula position should be an integral part of the assessment of patients who present with recurrent HF symptoms after LVAD implantation.

In our study, none of the other device position parameters were associated with unloading. However, it remains important to direct attention to these other parameters for the purpose of reducing the risk of pump thrombosis.[3] The majority of the patients in our study (91%) had an inflow cannula and pump angle above 55° (previous reports suggest that angles less than 55° increase the risk of pump thrombosis).[6] Importantly, none of the patients in our study experienced pump thrombosis.

Future Directions and Study Limitations

This study found that a narrower inflow cannula angle is a key factor in achieving adequate LV unloading and preventing HF readmissions. We did not identify any background factors associated with inflow cannula position, indicating that device position may be mostly dependent on surgical technique. Recent publications have outlined a specific approach to HeartMate II implantation,[3] and the results of this study support the argument for a standardized procedure that includes a meticulous focus on ensuring appropriate inflow cannula position. The ability to achieve ideal cannula position may be dependent on surgical experience, as well as anatomical features such as heart size and the anteroposterior diameter of the thorax.

This study has several limitations. This is a moderate-sized single-center study. CXR was assessed at a single time point, and we relied on the assumption that device position parameters except for pump depth do not change significantly over time.[5,6] The route of the outflow graft or the angle of outflow graft relative to the ascending aorta was not measured because of its lack of visibility on CXR, and thus we cannot assess the impact of outflow graft position on clinical outcomes.[13] We enrolled only clinically stable outpatients. The absolute value of PCWP, which we used as a surrogate marker of LV unloading, may change at specific condition such as aortic insufficiency and right ventricular failure. Lastly, in this study, we used only CXR for the assessment of device position instead of echocardiography or cardiac computed tomography, considering its convenience, noninvasiveness, cost-effectiveness, and objectiveness (inter-rater reliabilities of device parameter were all high).

Conclusion

HeartMate II LVAD inflow cannula position was associated with LV unloading and clinical outcomes. Our findings emphasize the importance of applying rigorous attention to inflow cannula position at the time of LVAD implantation.

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