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THOUGHTS & PROGRESS

Technology and technique for left ventricular assist device optimization: A Bi-Tech solution

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Abstract

Background: We investigated the synergistic effect of the new cone-bearing design of Jarvik 2000 (Jarvik Heart Inc., NY) together with a minimally-invasive approach to outcomes of LVAD patients.

Methods: We retrospectively reviewed all patients from 5 institutions involved in the Jarvik 2000 Italian Registry, from October 2008 to October 2016. Patients were divided into three groups according to pump design and implantation technique: pin-bearing design and conventional approach (Group 1); cone-bearing and conventional approach (Group 2); cone-bearing and minimally-invasive implantation (Group 3).

Results: A total of 150 adult patients with end-stage heart failure were enrolled: 26 subjects in Group 1, 74 in Group 2, and 50 in Group 3. Nineteen patients (73%) in Group 1, 51 (69%) in Group 2, and 36 (72%) in Group 3 were discharged. During follow-up, 22 patients underwent transplantation, while in 3 patients the LVAD was explanted. The overall 1-year survival was 58 ± 10%, 64 ± 6%, and 74% ± 7% in Groups 1, 2, and 3, respectively ($p = 0.034$). The competing-risks-adjusted cumulative incidence rate for adverse events was 42.1 [27–62.7] per 100 patient-years in Group 1, 35.4 [25.3–48.2] in Group 2, and 22.1 [12.4–36.4] in Group 3 ($p = 0.046$ for Group 1 vs. 3).

Conclusions: The association of the modern cone-bearing configuration of Jarvik 2000 and minimally invasive surgery improved survival and minimized the risk for cardiovascular events, as a result of combining technology and technique.

KEYWORDS

cone-bearing, Jarvik 2000, minimally-invasive

Deceased author.

1 | INTRODUCTION

The Jarvik 2000 (Jarvik Heart Inc., NY), a non-pulsatile axial-flow left ventricular assist device (LVAD), has recently approached the third decade of implants. As drawbacks of the growing experience, adverse events and modes of device failure became evident with time, especially the risk for thrombosis in the smaller versions.[1] These challenges generated the opportunity for constant and systematic optimization of the device, which finally led to its actual design.[2]

The ameliorations made to the pump consisted of a novel wire configuration of cables, a titanium microsphere coating of the intraventricular surface of the pump, an intermittent low-speed controller to permit aortic valve washout, and a novel cone-bearing design.[2,3]

Simultaneously, surgical techniques have progressed in the field of LVAD implantation, transforming a once pioneeristic operation into a routine procedure that can be achieved on the beating heart, off-pump, and through minimally invasive access.[4–6]

With the present work, we aimed to assess the combined effect of the modern cone-bearing *technology* of Jarvik 2000 and the minimally-invasive surgical *technique* on outcomes of patients undergoing LVAD implantation.

2 | MATERIALS AND METHODS

2.1 | Technology

The original design of the Jarvik 2000 featured a pin-bearing configuration, which was associated with circumferential thrombus formation at the pin-sleeve interface, raising concerns about a potential source for clot embolization.[1,2] In 2010, the Jarvik 2000 was upgraded with a novel cone-bearing design, where the rotating ceramic bearing cones are suspended in stationary seats, making contact with three short blades (Figure 1). These blades reduce friction and augment blood washing of the bearings, eliminating the circumferential interface where clots were seen to deposit.[1–3]

2.2 | Technique

Four different surgical approaches were adopted in this study: (1) a postero-lateral left thoracotomy with the outflow graft anastomosed to the descending aorta; (2) a full sternotomy with the outflow graft anastomosed to the ascending aorta; (3) a left anterior mini-thoracotomy in the fifth intercostal space for pump insertion in the left ventricular apex + an upper ministernotomy for outflow graft's anastomosis to the ascending aorta[4,5]; (4) a left anterior mini-thoracotomy in the fifth intercostal

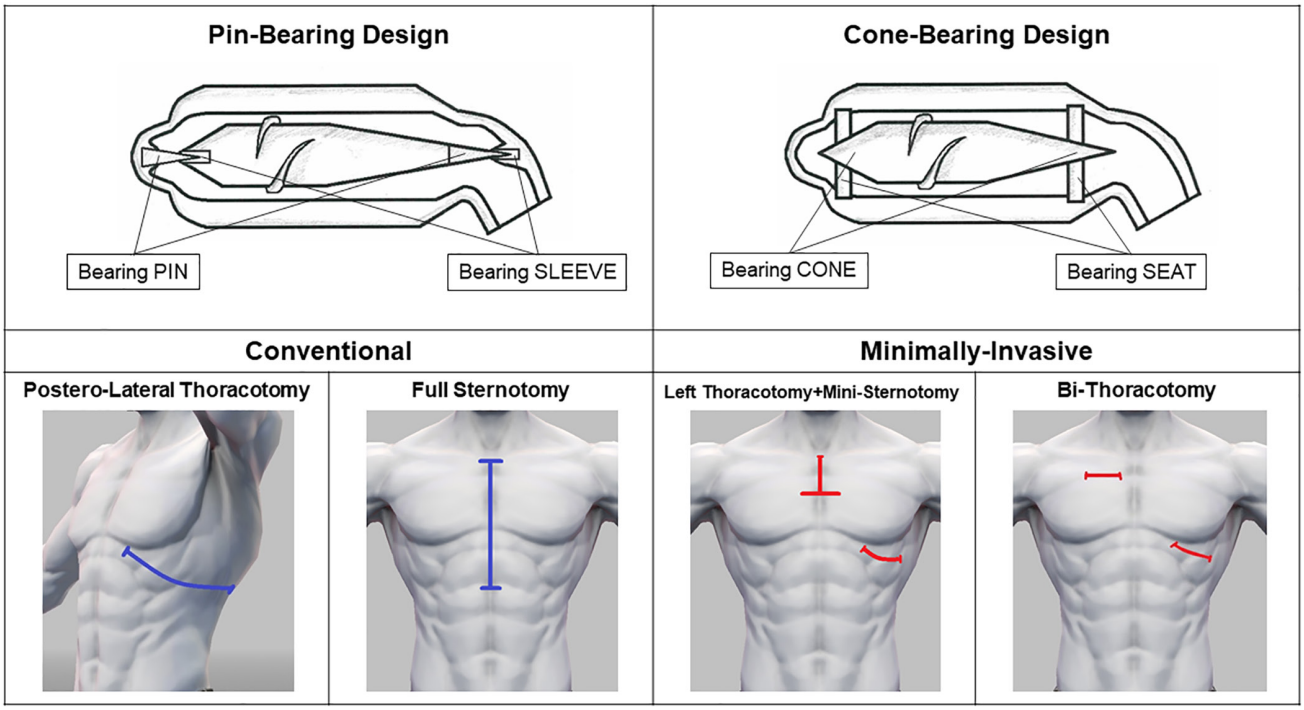

FIGURE 1 Different pump designs of Jarvik 2000 and surgical approaches for implantation.

space + a right anterior mini-thoracotomy in the second intercostal space for accessing the ascending aorta (bi-thoracotomy).[6] Since a mini-sternotomy or a bi-thoracotomy with limited skin incisions are proven to reduce tissue trauma, sources of bleeding and enhance postoperative recovery,[7,8] we investigated the specific effect of minimal-invasive surgical access on patients' outcomes. We referred to the first two techniques as *conventional* and the latter two as *minimally invasive* (Figure 1). All procedures were accomplished on the beating heart with ($n = 63$) or without ($n = 87$) cardiopulmonary bypass, depending on the hemodynamic stability of the patient and risk for ventricular arrhythmias during the implantation, and according to the surgeon's preference. The power delivery system was tunneled to a retroauricular skull pedestal in all cases.

2.3 | Population

We performed a retrospective review of adult patients from 5 institutions involved in the Jarvik 2000 Italian

TABLE 1 Baseline and intraoperative characteristics of patients

	Group 1 ($n = 26$)		Group 2 ($n = 74$)		Group 3 ($n = 50$)		
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	***p*-value**
Age (years)	61	8	61	8	60	10	0.855
Body surface area (m^2)	1.85	0.15	1.87	0.21	1.92	0.15	0.146
Left ventricular ejection fraction (%)	20.5	2	21	3.1	22	3	0.139
Cardiac index (L/min/m^2)	2.1	0.2	2.1	0.2	2	0.1	0.896
Creatinine (mg/dl)	1.5	0.3	1.6	0.4	1.7	0.3	**0.048**
Total bilirubin (mg/dl)	1.3	0.3	1.4	0.5	1.3	0.3	0.097
Hemoglobin (g/L)	11.2	1.8	11.0	1.7	10.9	1.5	0.762
Platelet count (10^3/μl)	210	10	220	18	216	19	0.129
	n	**%**	***n***	**%**	***n***	**%**	
Male	23	89	57	77	43	86	0.284
Etiology of heart failure							0.886
Dilated cardiomyopathy	11	42	36	49	26	52	
Ischemic cardiomyopathy	13	50	33	44	22	44	
Other	2	8	5	7	2	4	
Chronic kidney disease	8	31	25	34	16	32	0.954
Renal replacement therapy	2	8	3	4	3	6	0.704
Preoperative ECMO	2	8	3	4	5	10	0.415
Preoperative IABP	3	12	4	5	8	16	0.132
INTERMACS profile							**0.037**
Class 1–2	5	19	26	35	22	44	
Class 3–4	21	81	48	65	28	56	
Intention to treat							0.063
Destination therapy	25	96	51	69	29	58	
Bridge to candidacy	0		9	12	8	16	
Bridge to transplantation	1	4	14	19	13	26	
Thoracotomy	24	92	37	50	0		**<0.001**
Sternotomy	2	8	37	50	0		**<0.001**
Minimally-invasive approach	0		0		50	100	**<0.001**
Outflow in ascending aorta	2	8	40	54	50	100	**<0.001**
Outflow in descending aorta	24	92	34	46	0		**<0.001**
Off-pump Implantation	22	85	42	57	23	46	**0.006**

Bold value indicates statistical significance of $p < 0.05$.

Abbreviations: ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump.

TABLE 2 Adverse events and outcomes of patients

	Group 1 ($n = 26$)		Group 2 ($n = 74$)		Group 3 ($n = 50$)		
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	***p*-value**
LVAD support duration (months)	26	5	14	2	12	2	**0.001**
Follow-up (months)	27	6	19	2	16	2	0.062
Follow-up range (months)	[1–88]		[1–76]		[1–53]		
	n	**%**	***n***	**%**	***n***	**%**	
Discharged	19	73	51	69	36	72	0.837
Transplanted	0		13	18	9	18	0.067
LVAD removal	0		2	3	1	2	0.699
In-hospital mortality	6	23	17	23	4	8	**0.038**

	Incidence rate (per 100 patient-years)	**95% confidence interval**	**Incidence rate (per 100 patient-years)**	**95% confidence interval**	**Incidence rate (per 100 patient-years)**	**95% confidence interval**	***p*-value Group 1 vs. 2**	***p*-value Group 1 vs. 3**	***p*-value Group 2 vs. 3**
Pump thrombosis	1.8	[0.1–9.8]	3.5	[0.1–9.1]	1.5	[0.1–8.4]	0.911	1	0.785
Major bleeding	15.8	[7.2–30]	15	[8.8–24.1]	7.6	[2.5–17.7]	1	0.282	0.243
Ischemic stroke	12.3	[4.9–25.3]	15	[8.8–24.1]	7.6	[2.5–17.7]	0.825	0.587	0.243
Hemorrhagic stroke	8.8	[2.9–20.1]	6.2	[2.5–12.8]	4.5	[0.9–13.3]	0.752	0.575	0.925
Right ventricular failure	8.8	[2.9–20.1]	13.3	[7.4–21.9]	12.1	[5.2–23.9]	0.577	0.775	1
Sepsis	14	[6.1–27.7]	8	[3.6–15.1]	13.6	[6.2–25.9]	0.357	0.953	0.248
Bowel ischemia	0		0.9	[0.1–5]	4.5	[0.9–13.3]	1	0.308	0.291
Competing-risks-adjusted cumulative incidence rate of adverse events	42.1	[27–62.7]	35.4	[25.3–48.2]	22.1	[12.4–36.4]	0.501	**0.046**	0.115

Bold value indicates statistical significance of $p < 0.05$.

Registry, treated from October 2008 to October 2016. The patient's written informed consent was obtained, and the study was approved by local institutional Ethics Committees. Patients were divided into three groups according to pump design and implantation technique: pin-bearing design and conventional approach (Group 1, $n = 26$); cone-bearing design and conventional approach (Group 2, $n = 74$); cone-bearing design and minimally-invasive implantation (Group 3, $n = 50$). The primary end-point was cardiovascular-related mortality. Secondary end-points were the most significant adverse events.

2.4 | Statistical analysis

Data are summarized as mean ± standard deviation and counts and percentages, as appropriate. Comparisons between groups were made with the Kruskal-Wallis test and Fisher's exact test. Survival curves were estimated with Kaplan–Meier and compared with the log-rank test. To take into account the different follow-up times between groups, an exposure-adjusted incidence rate of adverse events was used and compared across groups with an exact (unbiased) rate ratio test assuming Poisson counts with given time (e.g., patient-years) at risk for each count. A competing-risk-adjusted analysis was performed to assess the cumulative incidence rate of adverse events. Analyses were performed using SPSS 23.0 (IBM Corporation, Armonk, NY) and R 4.2 (R core team).

3 | RESULTS

A total of 105 patients underwent LVAD implantation as destination therapy, 17 as a bridge to candidacy, and 28 as a bridge to transplantation. Baseline and intraoperative characteristics are summarized in Table 1. Of note, patients in INTERMACS classes 1–2 were more represented in Group 3 than in Groups 1 and 2 (44% vs. 19% and 35%, $p = 0.037$). An off-pump approach was adopted in 87 (58%) patients, mostly in Group 1 (85%) than Groups 2 and 3 (57% and 46%, respectively, $p = 0.006$).

Exposure-adjusted incidence rates of cardiovascular adverse events are presented in Table 2. The competing-risks-adjusted cumulative incidence rate for adverse events was 42.1 [27–62.7] per 100 patient-years in Group 1, 35.4 [25.3–48.2] in Group 2, and 22.1 [12.4–36.4] in Group 3 ($p = 0.046$ for Group 1 vs. 3, Table 2). In-hospital mortality resulted to be lower in Group 3 (8%) than in Groups 1 and 2 (23% and 23%, respectively, $p = 0.038$). After a mean follow-up of 19 ± 2 months, 22 patients were transplanted (13 from Group 2 and 9 from Group 3) and 3 patients recovered and the LVAD was explanted (2 from Group 2 and 1 from Group 3). One-year survival was 58 ± 10%, 64 ± 6%, and 74% ± 7% in Groups 1, 2, and 3, respectively ($p = 0.034$, Figure 2).

4 | DISCUSSION

The Jarvik 2000 emblematizes the progress made in the field of LVAD surgery during the three decades of its utilization. As problems and limits of this device have been identified, *technology* evolved, optimizing design and characteristics,[1–3] as well as surgical *techniques*.[4–6]

It has been already demonstrated that the introduction of the cone-bearing design has provided significant improvements in patients' survival and freedom from adverse events.[3] Similarly, reducing the invasiveness of implantation enhanced patients' recovery and shortened times of hospitalization.[7] However, no data are available on whether the combination of modern technology and technique may have a synergistic and additional effect on patients' prognosis.

In our work, we confirmed that the cone-bearing design, despite a more challenging population, represents a protective factor for major postoperative morbidities per se. In fact, our large multicenter cohort was composed of relatively old patients, in which the Jarvik 2000 implantation was intended as destination therapy in most cases. Furthermore, patients in higher INTERMACS classes were more represented in Groups

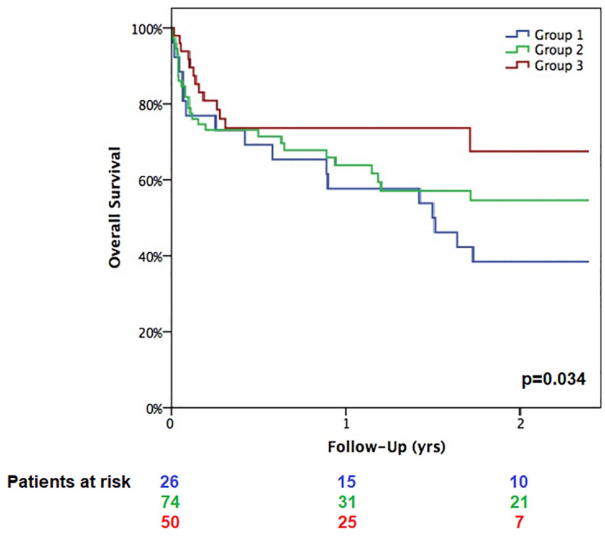

FIGURE 2 Kaplan–Meier plot of survival rate according to study groups.

2 and 3 (Table 1), delineating particularly complex cohorts. Despite these premises, the competing-risks analysis revealed that patients with new pump design experience a reduction in the incidence rate of complications (Table 2). Our results support the experimental in-vitro and in-vivo findings of enhanced resistance to clot formation around the suspending mechanism of the cone-bearing design.[1–3] However, the differences between the pin-bearing and cone-bearing designs could have been magnified by the non-availability of patients in which the pin-bearing pump was implanted with a minimally-invasive approach.

Furthermore, the impact of surgical techniques was investigated. The modality of implantation both contributed to a further decline (although not statistically significant, $p = 0.115$) in the incidence rate of adverse events among the cone-bearing design groups and affected patients' survival substantially. In fact, in-hospital mortality dropped from 23% in both Group 1 and 2 to 8% in Group 3 ($p = 0.038$), corroborating the hypothesis of an intrinsic beneficial role of the minimally-invasive access, even if off-pump implantation was adopted in most of the conventional techniques (Table 1), optimizing the perfusion technique for patients in Group 1. In fact, the inferior surgical trauma and the minimal exposition of anatomical structures are proven to reduce sources of bleeding and infections.[7,8] In addition, limited openings of the pericardium could play a role in reducing the risk of right ventricular failure.[7,8] In our experience, these advantages of the minimally-invasive approaches demonstrated to produce a beneficial effect on prognosis that overtook the drawback of a higher need for a cardiopulmonary bypass to perform the procedure safely.

As a result, combining modern *technology* and surgical *technique*, we enhanced the clinical outcomes of our patients exponentially, minimizing the risk for adverse events and ameliorating survival, which improved constantly from Group 1 to Group 2 and 3 ($58 \pm 10\%$, $64 \pm 6\%$, and $74\% \pm 7$ at 1 year, respectively, $p = 0.034$, Figure 2), consistently with data from the prospective Jarvik 2000 bridge to transplant investigational device exemption study.[9] In this view, every technological and surgical effort should be pursued to optimize patients' prognoses.

5 | CONCLUSIONS

In our large prospective multicenter cohort, the new cone-bearing design of Jarvik 2000 together with a minimally-invasive surgical approach displayed a synergistic protective effect on a patient's prognosis. Combining modern *technology* and surgical *technique* reduced significantly the risk for cardiovascular adverse events and in-hospital mortality, resulting in an additive improvement in patients' long-term survival.

AUTHOR CONTRIBUTIONS

Vincenzo Tarzia, Matteo Ponzoni, Lorenzo Bagozzi, Giacomo Bortolussi, Gino Gerosa conceived and wrote the article; Massimo Maccherini, Massimo Maiani, Piergiuseppe Agostoni, Daniele Marinelli, Anna Apostolo, Sonia Bernazzali, Helena Ortis, Michele Di Mauro, Silvia Scuri, Guido Sani, Tomaso Bottio, contributed to the final version of the manuscript. Gabriele Di Giammarco, Ugolino Livi, Francesco Alamanni, Gino Gerosa supervised the work.

CONFLICT OF INTEREST

S.S. is a consultant for ArTech srl (dealer of biomedical products, including Jarvik 2000). All other authors have no conflicts of interest to declare.

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