あるいは薬剤X誘導ヒト脂肪組織由来多系統前駆細胞移植は、重症心不全患者にとって新規治療となる可能性が示された。今後、より長期にわたる移植後経過観察による有用性の検証を行い、すみやかな薬事展開を目指したい。

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H. 知的財産権の出願・登録状況

1. 特許取得

大阪大学に発明届出書及び譲渡証明書を提出中。

2. 実用新案登録

なし

3.その他

なし

厚生労働科学研究費補助金（難治性疾患克服研究事業）

cGMP 対応の細胞培養システムの構築

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研究要旨

cGMP対応の細胞培養システムの構築

自己脂肪幹細胞を用いた再生医療の普及を図るためには、細胞培養施設（CPC）で製造される細胞製剤の薬事対応を担保するCPC図書群の作成が必須である。本研究では、CPC図書作成に必要な施設・製造・品質保証要件を検討する。

Ａ．研究目的

自己細胞を用いた再生医療の普及を図る為には、薬事対応のＣＰＣと書の作製が必須である。本研究では、CPCで実際の細胞培養を行いCPC図書作成に必要な標準管理基準書･手順書の作成を行った。

Ｂ．研究方法

先端医療センターが保有するCPCでヒト脂肪細胞を用いてCPC　Cold runを実施し、そのデータを用いて細胞製造・品質保証に必要なCPC図書を作成した。

（倫理面への配慮）

使用したヒト細胞は、個人情報の管理がされている試料を使用した。

Ｃ．研究結果

細胞培養後の出荷判定基準設定と逸脱時の手順設定はCPC図書における最重要項目の一つである。出荷判定基準自体のバリデーションと設定値の再設定が可能となるような文章体系を策定した。

Ｄ．考察

CPCでCold　Runを実施することで、実際の臨床に供する培養細胞の細胞規格と出荷判定基準の設定が可能となった。

Ｅ．結論

本研究では、幹細胞研究指針適合確認に基づく臨床研究、高度医療実施、それに続く医師主導治験を実施するうえで必要とされるCPC図書文書体系の提供を目指しており、わが国の再生医療研究の進展を促進するものと考える。

Ｆ．研究発表

１．論文発表

The use of leukemia inhibitory factor immobilized on virus-derived polyhedra to support the proliferation of mouse embryonic and induced pluripotent stem cells.
Naoki Nishishita, Hiroshi Ijiri, Chiemi Takenaka, Kenichiro Kobayashi, Kohei Goto, Eiji Kotani, Tohru Itoh, Hajime Mori, Shin Kawamata
Biomaterials, 2011 May, 32(14): 3555-3563

２．学会発表

なし

Ｇ．知的財産権の出願・登録状況（予定を含む）

１．特許取得

２．実用新案登録

３．その他

なし

厚生労働科学研究費補助金（難治性疾患克服研究事業）
研究分担報告書（平成23年度）

重症拡張型心筋症へのbridge-to-transplantation/recoveryを目指した心筋治療法の安全性・有効性評価のための生物統計学的デザイン・方法論の開発に関する研究

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研究要旨

重症拡張型心筋症へのbridge-to-transplantation/recoveryを目指した心筋治療法の開発のためのいくつかの臨床研究が実施されている．本分担研究では，当該臨床研究の実施計画書の作成に参画した経験を活かして，本治療法の効果に関する生物統計学的評価のためのデザイン，とくに，症例数設計の方法論を開発した．小規模の数値例を通じてその性能を評価し，実地での適用可能性を検討した．結果として，本研究で開発したデザインは，重症拡張型心筋症へのbridge-to-transplantation/recoveryを目指した心筋治療法の効果に関する臨床評価過程に相応に寄与することが示唆された．

A．研究目的

米国Food and Drug Administration (FDA) より医療機器の臨床試験におけるBayes流統計学の使用に関する指針 ``Guidance for the Use of Bayesian Statistics in Medical Device Clinical Trials" が提示されたが，この指針が提示されるに至るまでに，探索的臨床試験におけるBayes流デザイン及び統計的推測方式はすでに海外では注目・実践されており，我が国における適切な臨床評価の基盤の確立，その結果の患者への還元の視点からみても，国内でのその適用の必要性が叫ばれてきている．このことは，重症拡張型心筋症へのbridge-to-transplantation/recoveryを目指した心筋治療法の開発に関する臨床研究でも例外でなく，bridge-to-transplantation/recoveryという今目の前にいる患者さんを治療できる革新的な治療法の普及・確立には，適切な臨床評価の基盤を支える生物統計学的検討のためのデザインと統計解析のための方法論が必要になる．

前年度までは主に，安全性評価のためのデザイン及び統計解析の方法論に関する開発を行ってきたが，本年度では，心筋治療法の効果を評価するためのデザインを開発し，数値例を通じて実地でのその適用可能性を検討することを目的とした．とくに，ここでは，先述の指針の流れを受けて，既存の頻度流のデザインではなくBayes流のデザイン，とくに，症例数設計に関する開発を行うこととした．

B．研究方法

θを心筋治療法の効果に関する真の反応割合とし，Yはある患者に対して本治療法が成功すれば1，そうでなければ0をとる2値の確率変数とする．このとき，$S=\sum_{i=1}^{n} Y_i$は，治療が成功した患者数を表し，2項分布に従うと仮定できる．さらに，θにベータ事前分布を仮定すれば，Bayes流統計学ではよく知られるように，共役解析の結果としてθの事後分布はベータ分布であり，Sの予測分布はベータ2項分布に従うと仮定できる．

θ_0を本治療法に対峙する対照治療法や既存の標準的治療法についての反応割合の値（適切な文献値から同定される）とし，δをその反応割合に上乗せされる臨床的に意味のある効果の値，$\pi^{\mathrm{A}}(\theta)=\mathrm{Beta}(\theta;a^{\mathrm{A}},b^{\mathrm{A}})$を$\theta$の事前分布とする．

ここに，a^{A}及びb^{A}は事前に規定されるパラメータ値である．n例の患者の効果が観測されたもとで，真の反応割合θがθ_0よりも臨床的に意味のある程度(δ)大きくなる，つまり$\theta > \theta_0 + \delta$となる事後確率は$p_n(S) = \pi_n^A(\theta > \theta_0 + \delta \mid S)$で与えられる．この確率を用いると，事前に規定される閾値λに対して，本治療法の成功患者数sが$p_n(s) \geq \lambda$を満たせば，本治療法は有効であったと宣言することが可能である．この確率を症例数設計に活かすとき，その設計が試験計画時に行われるため，本研究では，この確率を予測分布$m^D(s) = \int_0^1 f_n(s \mid \theta)\pi^D(\theta)d\theta \quad \forall s = 0,...,n$上でとらえなおすことで症例数を算出することを提案する．ここに，$f_n(s \mid \theta)$はSの確率関数であり，$\pi^D(\theta) = \mathrm{Beta}(\theta; a^D, b^D)$は，本治療法がどの程度の反応割合をもつかを表す事前分布であり，$\pi_n^A(\theta)$とは別のデザインのために規定するものである．すなわち，事前に規定される閾値γに対して$\Pr^D[p_n(S) \geq \lambda] \geq \gamma$を満たすような$n$の最小値を算出し，これを計画している試験の必要な症例数とする．

（倫理面への配慮）

本研究で開発した統計的デザイン及び方法論は，心筋治療法の臨床試験において必要な症例数を算出するためのものであり，患者様から直接に得られた現実データには適用しておらず，倫理面への配慮は現時点では必要ないと考える．

C．研究結果

実際場面を想定して，$\theta_0 + \delta$=0.2, 0.3, 0.4, 0.5, 0.6, 0.7, $\pi^A(\theta) = \mathrm{Beta}(\theta;1,1)$(すなわち，無情報事前分布である)，$\pi^D(\theta) = \mathrm{Beta}(\theta;\infty,\infty)$，$\lambda = 0.8$，0.9，$\gamma = 0.7$，0.8 の場合に対して，本治療法の反応割合が，$\theta_0 + \delta$よりも 15%，20%上回ると期待される場合に必要な患者数を算出し，表に示した．

表内の上段及び下段の値はそれぞれ$\gamma = 0.7$，0.8 の場合の患者数であり，鍵括弧内は，帰無仮説$H_0 : \theta \leq \theta_0 + \delta$，対立仮説$H_1 : \theta \geq \theta_0 + \delta + 0.15$又は$H_1 : \theta \geq \theta_0 + \delta + 0.2$としたとき 2 項分布を仮定した仮説検定に基づいて算出される症例数である．ここで第 I 種の過誤は$\alpha = 1 - \lambda$，第 II 種の過誤は$\beta = 1 - \gamma$とした．

表に示されるように，$\pi^D(\theta) = \mathrm{Beta}(\theta;\infty,\infty)$を仮定すれば，Bayes 流の方法を用いて算出された必要な症例数は，通常の仮説検定に基づいて算出された必要な症例数よりも少なくてすむことがわかる．また，λとγが大きくなるほど，すなわち，仮説検定の枠組みで解釈すると過誤の確率を小さくすればするほど，また，本治療法が$\theta_0 + \delta$よりも上回る反応割合を期待できないほど患者数は増えることがわかる．

表. Bayes 流標本サイズの設計結果

	$(\theta_0+\delta)+0.15$		$(\theta_0+\delta)+0.20$	
$\theta_0+\delta$	λ=0.8	λ=0.9	λ=0.8	λ=0.9
0.2	16[26]	29[38]	9[17]	17[22]
	25[34]	41[47]	16[22]	22[30]
0.3	20[27]	34[41]	11[18]	20[24]
	29[36]	48[58]	17[24]	28[32]
0.4	24[26]	39[45]	15[16]	22[29]
	33[41]	48[58]	16[25]	28[34]
0.5	25[28]	41[44]	14[17]	23[26]
	36[41]	52[57]	18[24]	30[33]
0.6	23[27]	38[42]	15[16]	20[24]
	32[35]	46[53]	18[22]	26[30]
0.7	20[21]	32[33]	13[14]	15[21]
	28[29]	40[45]	17[18]	20[25]

D．考察

開発したデザインは，事後確率$p_n(s)$，又は$\pi^A(\theta)$から導出される事前予測分布上でこの確

率をとらえなおすことで得られる値が低い値を示せば，無効中止の観点から試験を早期中止することが可能である．逆に，それらが高い値を示せば，有効中止の観点から試験を早期中止することも可能である．

また，研究結果に示されるように，Bayes 流の方法で算出した症例数は，通常の仮説検定に基づいて算出した症例数よりも少ない．このことは，試験実施のためのコストの問題を減らし得る．開発したデザインは，この点では魅力的な方法といえる．ただし，ここでは示していないが，デザインのために規定する事前分布 $\pi^{\mathrm{D}}(\theta)$ の a^{D} 及び b^{D} の値を小さくしていくと，必要な症例数は増大していき，仮説検定に基づく場合の症例数を超えることに注意したい．それ故，本デザインを実地で適用するためには，a^{D} 及び b^{D} の値の臨床家からの定型的な導引方法の開発が今後の課題となる．

E．結論

本研究では，心筋治療法の効果を評価するためのデザインとして，Bayes 流の例数設計の方法を開発し，小規模の数値例でその性能を評価した．ここで開発した方法は，先述のようにデザインのための事前分布のパラメータ値の導引方法など解決すべき難点が残されており，国内外の生物統計家らとともに現在も精錬段階にある．これら諸種の難点が克服されれば心筋治療法の生物統計学的評価において新たな礎を与えると考えられる．

F．研究発表

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G．知的財産権の出願・登録状況(予定を含む)

1. 特許取得

該当せず.

2. 実用新案登録

該当せず.

3. その他

該当せず.

別紙４

研究成果の刊行に関する一覧表

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CASE REPORT

Implantation of a Jarvik 2000 left ventricular assist device as a bridge to eligibility for refractory heart failure with renal dysfunction

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Abstract A 55-year-old man, who previously underwent surgical ventricular restoration and mitral valve surgery, was referred to our department for management of refractory heart and multiple organ failure. At the time of admission to our hospital, he could not be registered as a candidate for heart transplantation because of severe renal failure with a serum creatinine level of 4.6 mg/dl. We considered that he was a marginal candidate for heart transplantation; thus, it was essential to understand the etiology of renal failure and estimate whether it was reversible. Cardiac catheterization revealed poor hemodynamic function with a systemic pressure of 107/60 mmHg, cardiac index of 2.5 l/min/m^2, and pulmonary artery pressure of 63/27 mmHg, despite intense medical treatment. Contrary to biochemical examination findings of blood, renal biopsy findings showed no significant glomerular abnormality. Furthermore, the severity of tubular atrophy and interstitial fibrosis in the cortex was mild. These pathological findings suggested that the renal dysfunction in this case was possibly attributable to a hemodynamic factor. His symptoms gradually deteriorated despite an increasing dose of inotropic support; thus, we planned implantation of a Jarvik 2000 axial-flow pump (Jarvik Heart Inc., New York, NY, USA) as a bridge to eligibility, and informed consent was obtained. Because of a tight adhesion on the anterior wall, we placed the device on the lateral wall of the left ventricle, making sure not to direct the pump at the septum. Postoperatively, the implantable left ventricular assist device provided relief from heart failure symptoms as well as recovery of renal function, with serum the creatinine level at 1.2 mg/dl, which allowed the patient to become an appropriate candidate for heart transplantation. At an 18-month follow-up examination, his status was uneventful, and he is now at home awaiting heart transplantation.

Keywords Jarvik 2000 · Left ventricular assist device · Renal dysfunction · Heart transplantation · Cardiomyopathy

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Introduction

Although the gold standard therapy for end-stage heart failure remains heart transplantation, this is not an option for patients with irreversible renal dysfunction, which is often complicated with advanced heart failure [1]. Herein, we report a patient complicated with renal dysfunction who underwent successful implantation of a Jarvik 2000 left ventricular assist device (LVAD) (Jarvik Heart Inc., New York, NY, USA) as a bridge to eligibility for refractory heart failure.

Case report

A 55-year-old man, who was diagnosed with idiopathic dilated cardiomyopathy on the basis of myocardial biopsy

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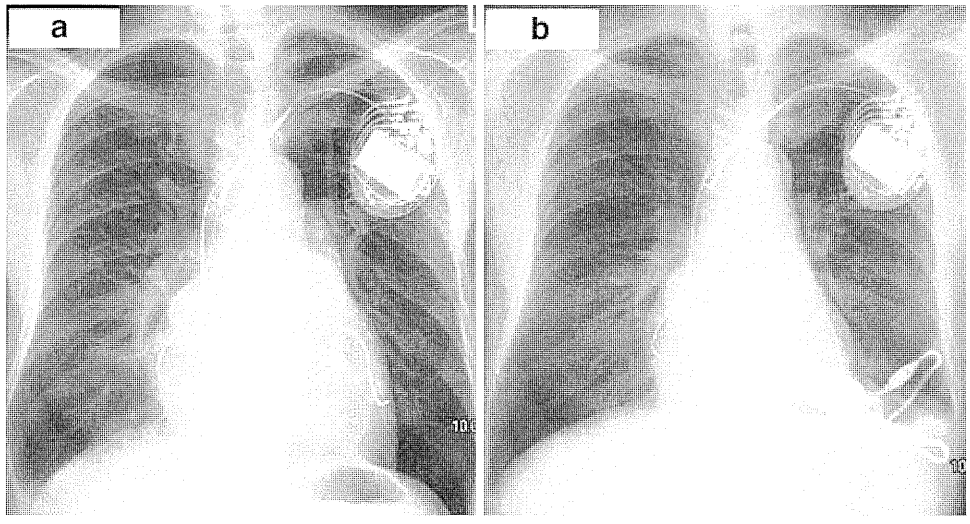

Fig. 1 **a** Chest X-ray image obtained before surgery showing pulmonary congestion and cardiomegaly with a cardio-thoracic ratio of 55%. **b** Chest X-ray image obtained at 1 month after surgery showing the Jarvik 2000 pump in an appropriate position, as well as relief of pulmonary congestion and absence of cardiomegaly

findings in 1995, underwent septal anterior ventricular exclusion (SAVE) and papillary muscle approximation for advanced left ventricular (LV) remodeling (end-systolic volume index 90 ml/m^2) in 2005. He also underwent mitral valve repair for severe functional mitral regurgitation at the time of the SAVE operation, followed by mitral valve replacement with a mechanical valve for recurrent mitral regurgitation in 2008, which did not improve the heart failure symptoms. The patient was referred to our institution on March 2009 for further management of sustained heart failure refractory to maximum pharmacological treatment and cardiac resynchronization therapy. On admission, he exhibited biventricular heart failure symptoms with pitting edema and peripheral coldness. Chest X-ray findings revealed pulmonary congestion and cardiomegaly with a cardio-thoracic ratio of 55% (Fig. 1a), while echocardiographic findings showed advanced left ventricular remodeling with an LV end-diastolic dimension of 75 mm and ejection fraction of 15%. A biochemical examination of blood showed multiple organ failure with serum creatinine at 4.6 mg/dl, blood urea nitrogen at 106 mg/dl, total bilirubin at 4.4 mg/dl, and brain natriuretic peptide at 637 pg/ml. A test of renal function also revealed a low endogenous creatinine clearance of 11.3 ml/min and high urinary fractional excretion of sodium of 3.0%, while neither urinary protein nor urinary occult blood were seen in urinalysis. The patient could not be registered as a candidate for heart transplantation at the time of admission, because of severe renal dysfunction. As the patient had a strong desire to spend his time at home and clearly refused to undergo implantation of a para-corporeal Toyobo LVAD (Nipro, Tokyo, Japan), we in consultation with cardiologists initiated administration of inotropic agents to improve cardiac function and determine whether hemodynamic improvements would result in improvement of the multiple organ failure.

Total bilirubin decreased from 4.4 to 1.1 mg/dl after beginning administration of the inotropic agents, while serum creatinine slightly decreased from 4.6 to 2.9 mg/dl and did not show signs of further improvement. Cardiac catheterization revealed poor hemodynamic function with a systemic pressure of 107/60 mmHg, cardiac index of 2.5 l/min/m^2, and pulmonary artery pressure of 63/27 mmHg, despite intense medical treatment. Renal sonography showed that both kidneys were of normal size and normal renal cortex echogenicity. It also showed no evidence of hydronephrosis, suggesting the absence of postrenal renal dysfunction. Microscopic findings from the renal biopsy revealed no significant glomerular change (Fig. 2a). Furthermore, the severity of tubular atrophy and interstitial fibrosis in the cortex was mild (Fig. 2b), which was not compatible with the findings of biochemical examination findings of blood. In other words, these pathological findings suggested that the renal dysfunction in this case was possibly attributable to a hemodynamic factor. His symptoms gradually deteriorated despite increasing the dose of inotropic support; thus, we planned to implant an implantable LVAD (Jarvik 2000) via a left thoracotomy. We explained to the patient and his family that he was a marginal candidate for heart transplantation, and they agreed to treatment with LVAD implantation as a bridge to eligibility, that is, possibly for transplantation or as destination therapy.

Under routine hemodynamic monitoring and double-lumen endotracheal intubation, a left thoracotomy was made through the seventh intercostal space, and the heart and distal part of the descending thoracic aorta were exposed. The anterior part of the heart was firmly adhered to the chest wall because of previous open heart surgery procedures. As the apex of the left ventricle could not be used as the coring site, because of the tight adhesion, we planned to place the Jarvik 2000 pump on the lateral wall

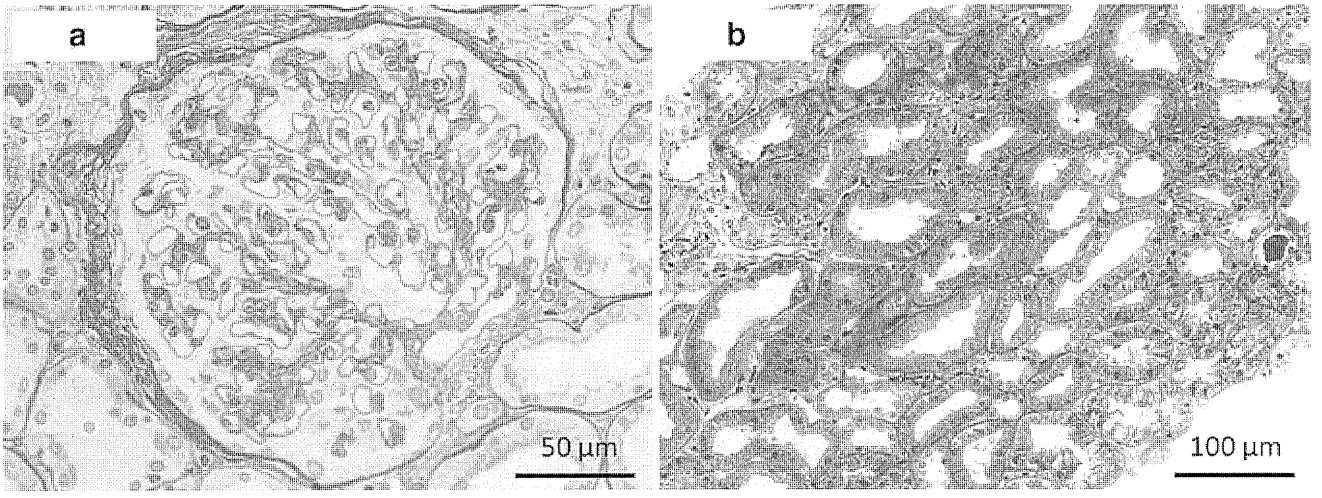

Fig. 2 **a** Periodic acid-Schiff staining results (at ×400 magnification) showing no evidence of significant glomerular change. **b** Elastica-Masson staining results (at ×200 magnification) showing mild tubular atrophy and interstitial fibrosis in the cortex

of the left ventricle. The pericardium was opened between the felt strip of the previous surgical ventricular restoration and left phrenic nerve. The heart was severely dilated, and there was sufficient area for LV coring in the lateral wall of the left ventricle. Following systemic heparinization, a partial cardiopulmonary bypass was established through a femoro-femoral bypass. The aorta was partially occluded, while the outflow graft was anastomosed to the descending aorta in an end-to-side fashion. The anterior part of the LV lateral wall was cored with a coring knife, with no thrombus found within the left ventricle. The Hemashield patch placed during the previous SAVE operation, and reconstructed anterior and posterior papillary muscles could be identified. A sewing cuff was sewn to the lateral wall of the left ventricle, and then the device was introduced into the left ventricular cavity through the sewing cuff, making sure not to interfere with the Hemashield patch or papillary muscles. As the cardiopulmonary bypass was gradually discontinued, the Jarvik 2000 pump was turned on. Hemodynamics were stabilized with an inotropic agent and pulmonary vasodilators.

Postoperatively, the implantable LVAD provided relief of heart failure symptoms, and inotropic agents were promptly discontinued 1 week after surgery. The endogenous creatinine clearance and serum creatinine level improved from 33.0 to 67.5 ml/min and 2.9 to 1.2 mg/dl, respectively, along with increased urine output. Chest X-ray findings at 1 month after surgery revealed that the Jarvik 2000 pump was in an appropriate position, as well as relief of pulmonary congestion and absence of cardiomegaly (Fig. 1b). Postoperative echocardiography findings showed remarkable unloading of the left ventricle (LV end-diastolic dimension 64 mm) as well as normal function of the mitral mechanical valve. At an 18-month follow-up examination, the status of the patient was uneventful, and he is at home awaiting heart transplantation at the time of writing.

Discussion

Axial flow pumps are generally smaller devices than the pulsatile pumps and may be associated with a lower incidence of complications [2–5]. Because of its small size, the Jarvik 2000 pump can be placed within the left ventricle, avoiding the need for an inflow cannula, while the outflow graft can be connected to either the ascending or descending aorta. Frazier et al. [6] reported their initial clinical experience with the Jarvik 2000 LVAD for patients with advanced heart failure, and found that it was safe and satisfactory to provide significant unloading of the left ventricle, resulting in improvements of hemodynamic parameters and functional status. In the present case, we selected this device with particular consideration given to the small body size of our patient (body mass index 17.8 kg/m^2) as well as his clinical history of open heart surgery procedures, both via a median sternotomy. Application of a left thoracotomy enabled us to avoid dissection of the anterior part of the heart and safely place the Jarvik 2000 pump on the lateral wall of the left ventricle. Implantation of a Jarvik 2000 pump through the lateral wall of the left ventricle might be suitable for patients with a history of surgical ventricular reconstruction. However, considerable attention must be paid to not directing the pump toward the septum, which may cause unstable blood removal and inadequate systemic perfusion.

Although the gold standard therapy for end-stage heart failure remains transplantation, this is not an option for patients with irreversible renal dysfunction, which often accompanies advanced heart failure [1]. If the

contraindications for cardiac transplantation are reversible (e.g., hepatic failure, renal failure), an LVAD can be very beneficial for stabilizing these patients and may serve as a bridge to eligibility for transplantation. The most important point of this report may be the expectation of reversibility of renal function by LVAD use in a marginal candidate for heart transplantation. This issue is quite important, especially in Japan where an implantable LVAD can be used only for approved heart transplantation candidates. In our case, the Jarvik 2000 LVAD provided significant improvement of renal function, which allowed the patient to become an appropriate candidate for heart transplantation. We speculated that several of the preoperative findings support the notion that some improvement in renal function could be anticipated after LVAD implantation. First, cardiac catheterization revealed advanced heart failure accompanied by low output syndrome, which indicated an etiology of secondary prerenal failure due to decreased renal perfusion. Possible explanations for improved renal function with LVAD support include improved cardiac output along with increased perfusion of the kidneys, as well as correction of neurohormonal dysregulation associated with congestive heart failure [7]. Second, the present urinalysis demonstrated no evidence of proteinuria, which is recognized as an important risk factor for progression of chronic kidney disease [8, 9]. Third, our patient had no history of diabetes mellitus or hypertension, which several authors have reported to be predictors of improvement of renal function following LVAD implantation. Sandner et al. [10] reported that absence of diabetes was the most important predictor of improvement of renal function following continuous LVAD implantation. Similarly, Butler and colleagues [11] showed that absence of diabetes, lower cardiac output prior to implantation, and lower body mass index, which were also observed in our patient, each had an association with improved renal function after pulsatile LVAD implantation. Additionally, another study showed a strong graded relationship between blood pressure and progression to end-stage renal disease [12]. These findings suggest that patients without structural kidney disease secondary to diabetic nephropathy or nephrosclerosis may be more likely to gain improved renal function after LVAD implantation. Indeed, the renal biopsy results showed no findings of obvious diabetic nephropathy, nephrosclerosis, or glomerulonephritis. We recommend that renal biopsy is useful to clarify the etiology of renal dysfunction. However, other studies are mandatory to confirm the usefulness of renal biopsy to determine the outcome of renal function following LVAD implantation in patients with these conditions.

In summary, we report successful implantation of a Jarvik 2000 LVAD as a bridge to eligibility for a patient with refractory heart failure complicated with renal dysfunction. Close collaboration with well-trained cardiologists or nephrologists is mandatory to evaluate the patient's organ function accurately and make more careful patient selection.

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Conflict of interest There are no conflicts of interest to report.

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CASE REPORT

Exchange of DuraHeart left ventricular assist device via a subcostal approach

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Abstract We report a successful case of a DuraHeart left ventricular assist device (LVAD) exchange via a subcostal approach. A 35-year-old woman was implanted with a DuraHeart LVAD due to dilated cardiomyopathy. Approximately 8 months after the implantation, the magnetic levitation system failed. The DuraHeart LVAD was exchanged emergently. The pump was freely dissected via a subcostal approach, avoiding redo sternotomy. De-airing of the new pump and the left ventricle was carefully performed. When the systemic flow was transferred from the cardiopulmonary bypass to the DuraHeart LVAD, an adequate flow was not initally obtained. Positional correction of the inflow conduit was needed to obtain full systemic flow. The postoperative course was uneventful. She was successfully discharged and is waiting at home for a heart donation.

Keywords DuraHeart · Device exchange · Subcostal approach

Introduction

A continuous-flow ventricular assist device (VAD) has recently been developed for the treatment of advanced heart failure. Effective hemodynamic support and excellent long-term results have been reported upon the application of the device [1, 2]. The DuraHeart left ventricular assist device (LVAD) (Terumo Heart, Inc., Ann Arbor, MI, USA) is the world's first magnetically levitated centrifugal blood pump. The European experience suggests that the DuraHeart LVAD can provide safe and reliable long-term circulatory support with both improved survival and acceptable adverse event rates in patients with advanced heart failure [3]. The excellent reliability and durability of the DuraHeart LVAD are beneficial for Japanese patients with severe heart failure, because the average waiting time for heart transplantation in Japan is more than 800 days. The potential for device malfunction increases with prolonged use of the LVAD. Prompt and appropriate management of device failure is essential to prevent lethal complications. We herein report our experience with the failure of a DuraHeart pump exchange.

Clinical summary

The patient was a 35-year-old woman with a diagnosis of dilated cardiomyopathy. She suffered from heart failure and was treated with β blocker and ACE inhibitor. However, her condition suddenly deteriorated due to exaggerated heart failure, and her hemodynamics was supported by extracorporeal devices. A Toyobo paracorporeal LVAD (Toyobo-Nipro, Osaka, Japan) was implanted emergently, and the patient was listed as a potential heart transplant recipient.

During the postoperative course, an ischemic stroke occurred. Fortunately, the patient recovered without any significant neurologic sequelae. In addition, mobile pump thrombi were often detected, and several paracorporeal pump exchanges were required during a short postoperative

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