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EXPERIMENTAL EN BLOC HEART–LUNG TRANSPLANTATION IN SWINE: INITIAL EXPERIENCE IN VIETNAM

Tuan Anh Ngo[1], Van Vien Mai[1], Vi Hai Ngo[1], Quoc Hung Nguyen[1], Huy Hieu Dao[1], Tien Dong Nguyen[1], Quang Thai Tran[1], Anh Tuan Hoang[1], Cong Hieu Dang[1], Hoai Nam Ha[1*]

[1]108 Military Central Hospital

*** Corresponding Author**
Hoai Nam Ha
Department of Cardiovascular Surgery, Heart Institute, 108 Military Central Hospital
E-mail: hahoainam29@gmail.com

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ABSTRACT

Objective: To describe the surgical technique and early outcomes of experimental en bloc heart-lung transplantation in swine at 108 Military Central Hospital. **Materials and methods:** This prospective experimental case series comprised three transplant procedures performed in 2021. Each procedure involved an organ donor, a recipient, and a blood donor. The heart–lung bloc was procured, preserved under cold conditions, and implanted through a median sternotomy using cardiopulmonary bypass (CPB). Four anastomoses were constructed: the tracheal, inferior and superior vena caval, and aortic anastomoses. Operative times, hemodynamics, blood gases, echocardiographic findings, coagulation parameters, and postoperative survival were analyzed descriptively. **Results:** Five technical protocols were developed, and all three transplantations were technically successful. Mean operative time was 233.3 ± 50.3 minutes, CPB time was 160.3 ± 46.8 minutes, aortic cross-clamp time was 81.0 ± 9.5 minutes, and cold ischemic time was 17.0 ± 2.6 minutes. All three graft hearts resumed beating; left ventricular ejection fraction after CPB discontinuation ranged from 70% to 85%. At two hours postoperatively, PaO_2 was 81-90 mmHg at an FiO_2 of 0.60, corresponding to PaO_2/FiO_2 ratios of 135-150 mmHg. One recipient required re-exploration for bleeding; postoperative bleeding and coagulopathy were documented in the study report. All three recipients died at 180, 325, and 370 minutes after surgery. **Conclusion:** To our knowledge, 108 Military Central Hospital is the first institution in Vietnam to perform experimental en bloc heart–lung transplantation. Five protocols provided a framework for coordination among animal preparation and logistics, anesthesia, perfusion, surgical, and postoperative intensive care teams. Technical success in three cases, with survival of approximately 3-6 hours, provides an experimental foundation for further development.

Key words: en bloc heart-lung transplantation; experiment transplantation; cardiopulmonary bypass; bicaval technique.

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1. Introduction

En bloc heart–lung transplantation replaces the heart and both lungs simultaneously in selected patients with end-stage cardiopulmonary disease. The work of Reitz et al. established the clinical feasibility of this procedure [1]. The 2021 International Society for Heart and Lung Transplantation (ISHLT) consensus emphasizes the comprehensive assessment of risk factors and appropriate timing of referral to a transplant center [2]. Developing a transplant program requires surgical expertise together with effective organ preservation, coordination of multiple teams, and post-reperfusion critical care.

The swine model permits surgical training with organs of a size suitable for adult cardiac surgical instruments, although relevant anatomical differences must be recognized [3]. Experimental transplantation is valuable both for practicing anastomotic techniques and for identifying factors that limit sustained graft function. Based on three transplant procedures performed at 108 Military Central Hospital, this article describes en bloc heart–lung transplantation using a bicaval technique, reports early outcomes, and examines areas requiring improvement.

2. Materials and Methods

2.1. Study design and animals

This prospective experimental case series was conducted at the Department of Experimental Medicine, 108 Military Central Hospital. Three procedures were performed in 2021. The results of organ procurement, flushing and preservation, and recipient cardiorespiratory explantation and graft implantation were published in two articles in 2023 [4,5]; the final study report was completed in 2025. The present article synthesizes the same three cases and includes no additional transplant procedures. Each procedure involved three pigs: an organ donor, a recipient, and a blood donor. Animals used in the same procedure were selected from the same herd and had comparable body weights. This was a feasibility series without a control group or randomization.

The six organ donors and recipients weighed 68–73.5 kg. Before surgery, the animals were housed and assessed according to the study protocol. Preoperative evaluation included general health assessment, hematological and biochemical testing, blood gas analysis, echocardiography, and radiography.

2.2. Preparation and preservation of the heart–lung bloc

The procurement and implantation teams worked in nearby operating rooms. General anesthesia with endotracheal intubation was administered, and an arterial line for blood pressure monitoring, intravenous access, and central venous pressure monitoring were established. Agents documented for maintenance of anesthesia and neuromuscular blockade included propofol, fentanyl, and atracurium. Vasopressors and inotropes were administered according to the hemodynamic course.

In the donor, a median sternotomy was performed, both pleural cavities were opened, and the aorta, venae cavae, and trachea were exposed. After anticoagulation, the heart–lung bloc was flushed with cold Custodiol solution through the aortic root and pulmonary trunk according to the study protocol. The graft was procured en bloc, inspected for parenchymal injury, and preserved at approximately 2-4°C after preparation of the vascular ends. The procurement report stated that all three grafts met the macroscopic criteria for transplantation. The intervals from the start of surgery to removal of the graft from the chest were 83, 86, and 90 minutes, respectively; flushing, anastomotic preparation, and graft inspection required 20, 16, and 15 minutes [4].

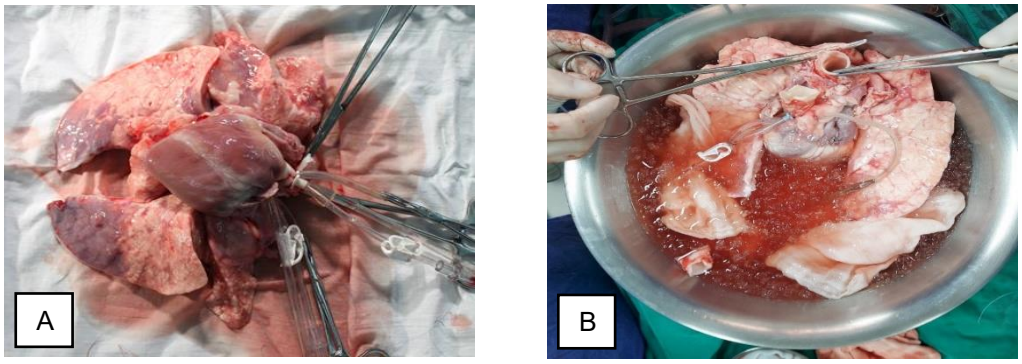


Figure 1. The heart–lung bloc after procurement (A) and graft inspection and preparation during preservation (B)

2.3. Data collection and analysis

Data were obtained from the final study report and its summary. Individual values were used, where available, to recalculate means and sample standard deviations (SDs; denominator n − 1). Parameters available only as aggregate data were retained as reported, with their source identified. Given the small sample size, no hypothesis testing or inferential assessment of efficacy was performed. The PaO_2/FiO_2 ratio at two hours was calculated from the blood gas and FiO_2 values for each case. Histopathological information for pig NC14 was obtained from the Department of Pathology report on hematoxylin-eosin-stained heart and lung specimens; these findings were restricted to the documented case and were not extrapolated to all three recipients.

2.4. Implantation technique and postoperative monitoring

A median sternotomy was performed in the recipient. Following heparinization, CPB was established using aortic and bicaval cannulation. The protocol specified hypothermia at 28-30°C and a pump flow of 2.0-2.4 L/m²/min. The native heart–lung bloc was removed while preserving the pericardial pedicles containing the phrenic nerves. The vascular and tracheal ends were prepared, and meticulous hemostasis of the dissection surfaces was achieved before graft placement.

The graft was positioned in the correct orientation within the chest, with both lungs arranged to prevent hilar torsion. The tracheal anastomosis was performed first because of its deep location and the difficulty of accessing it after completion of the vascular anastomoses. The report described a continuous suture technique using 3-0 polypropylene. End-to-end anastomoses of the inferior vena cava, superior vena cava, and aorta were then constructed. In the third case, the sequence was modified to trachea → inferior vena cava → aorta → reperfusion → superior vena cava. This was a modification within the series rather than a uniform sequence used in all three cases.

With en bloc transplantation of the heart and both lungs, the native connections between the heart and lungs within the graft are preserved; the four implantation anastomoses therefore do not include a separate pulmonary artery or left atrial anastomosis. After inspection, de-airing, and aortic unclamping, ventilation was resumed, circulatory support was provided, and cardiac function and readiness for reduction of CPB support were assessed. Preservation of the phrenic nerves, preparation of the recipient bed, and inspection of the anastomoses are important elements of the described heart–lung transplantation technique [6].

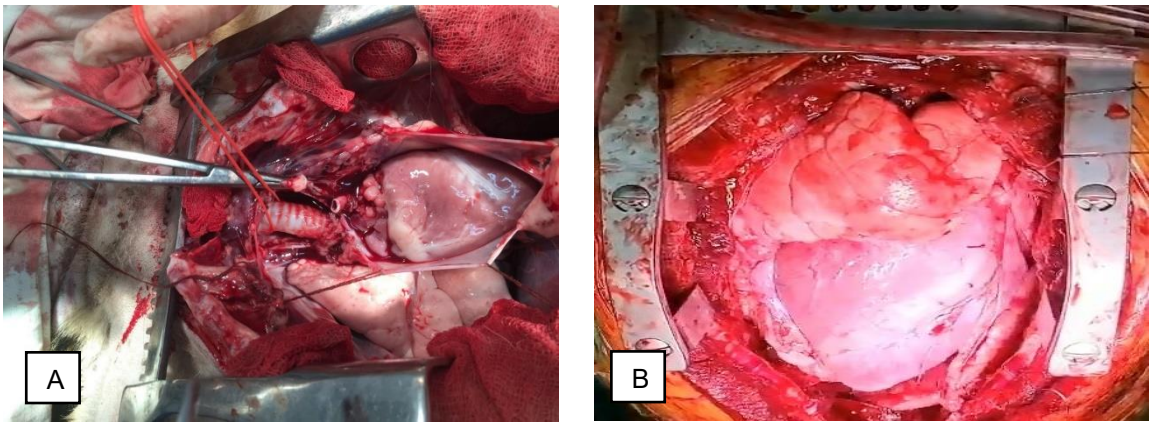


Figure 2. Construction of the aortic anastomosis (A) and the implanted heart–lung bloc (B).

Hemodynamics and blood gases were monitored at T1, after induction of anesthesia; T2, before CPB; T3, after aortic unclamping; T4, after CPB discontinuation; T5, before transfer to intensive care; and T6, 60 minutes after transfer to intensive care. Findings at two hours postoperatively are presented separately. The study criteria included resumption of cardiac activity, sinus rhythm, functioning cardiac chambers and valves, lung expansion, airway patency, $PaO_2 \geq 75$ mmHg, and $PaCO_2 \leq 45$ mmHg at an FiO_2 of 60% for at least 10 minutes. These criteria represent early graft activity and do not establish long-term survival or normal pulmonary function.

3. Results

3.1. Animal characteristics and operative times

Five protocols were developed, covering preparation; anesthesia and resuscitation; organ procurement, flushing, and preservation; recipient explantation and graft implantation; and postoperative intensive care. All three implantations were completed using the bicaval technique. Mean body weight of the six organ donors and recipients was 70.8 ± 2.5 kg; paired data are presented in Table 1.

Table 1. Characteristics of organ donors and recipients

Characteristic	Pair 1	Pair 2	Pair 3
Donor / recipient sex	Female / Female	Male / Female	Male / Male
Donor weight (kg)	70.0	72.0	68.0
Recipient weight (kg)	73.5	73.5	68.0
Recipient − donor weight (kg)	3.5	1.5	0.0
Same herd, as documented	Yes	Yes	Yes

Construction of the four anastomoses required 25, 34, and 37 minutes, respectively. The third case had the longest CPB duration and the longest period of CPB support during weaning. Cold ischemic time was only 15-20 minutes because the two operating rooms were located close to each other; these conditions do not reflect interhospital organ transport. Individual operative times and summary statistics are shown in Figure 3.

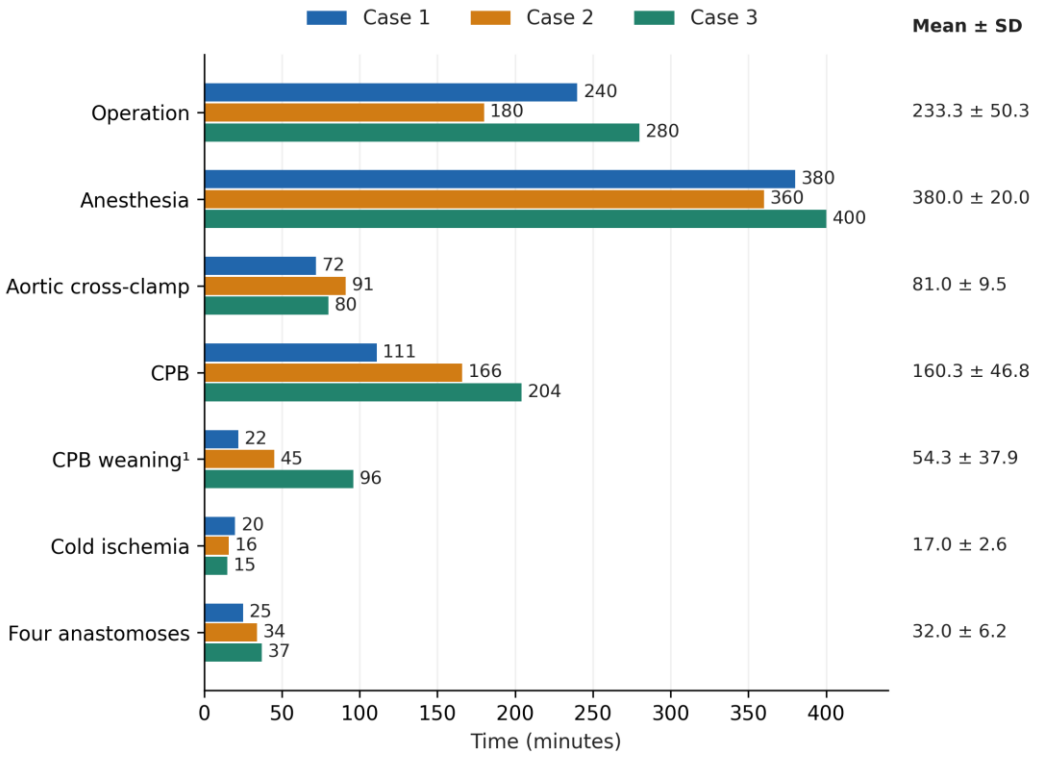


Figure 3. Operative and circulatory support times in the three cases. Labels show individual values; summary values are mean ± SD (n = 3). ¹CPB weaning time as reported in the published article. CPB, cardiopulmonary bypass

3.2 Early graft activity

All three graft hearts resumed beating within 3–5 minutes after aortic unclamping. Cardiac activity resumed spontaneously in cases 1 and 3, whereas case 2 required two electrical shocks. Ejection fraction (EF) after CPB discontinuation was 70%, 73%, and 85%, respectively. In case 3, mean arterial pressure immediately after unclamping was 49 mmHg and subsequently increased to 71 mmHg at the time point recorded as after CPB discontinuation. A photograph in the records documented central

ECMO in case 3. However, the absence of information on the timing, flow rate, and duration of support precludes confirmation of the extent to which graft function was independent of mechanical support in this case.

3.3 Hemodynamic and blood gas trends

Table 2. Hemodynamics and blood gases at the specified monitoring time points

Parameter	T1	T3	T4	T6
MAP (mmHg)	91.3 ± 1.5	66.0 ± 14.7	84.3 ± 11.6	63.3 ± 4.2
Heart rate (beats/min)	112.3 ± 2.5	125.0 ± 8.7	134.3 ± 18.6	145.0 ± 5.0
pH	7.40 ± 0.08	7.26 ± 0.10	7.28 ± 0.08	7.20 ± 0.09
PaO_2 (mmHg)	88.0 ± 67.4	148.5 ± 101.2	279.3 ± 67.8	112.5 ± 112.3
$PaCO_2$ (mmHg)	46.0 ± 7.5	44.0 ± 8.2	43.4 ± 5.6	41.2 ± 7.9

Note: Data are presented as mean ± standard deviation (SD; n = 3). Monitoring time points: T1, after induction of anesthesia; T2, before cardiopulmonary bypass (CPB); T3, after aortic unclamping; T4, after CPB discontinuation; T5, before transfer to intensive care; T6, 60 minutes after transfer to intensive care (data at T2 and T5 were not included in the summary table). Abbreviations: CPB, cardiopulmonary bypass; MAP, mean arterial pressure; PaO_2, arterial partial pressure of oxygen; $PaCO_2$, arterial partial pressure of carbon dioxide.

Blood pressure decreased after reperfusion, improved at T4, and declined again at T6, while heart rate increased. Mean pH decreased from 7.40 at T1 to 7.20 at T6. The report also documented an increase in mean lactate from 1.5 to 7.5 mg/dL between these time points. Because the source table did not specify the units, this finding was interpreted only as a trend and was not treated as standardized quantitative data for comparisons across studies.

At two hours, the individual blood gas values yielded calculated PaO_2/FiO_2 ratios of 138.3, 150.0, and 135.0 mmHg. Thus, although the study-defined PaO_2 threshold was met, oxygenation remained impaired. Bronchoscopy showed a patent airway without retained secretions. Chest radiography showed expanded lungs, with no documented pneumothorax or hemothorax.

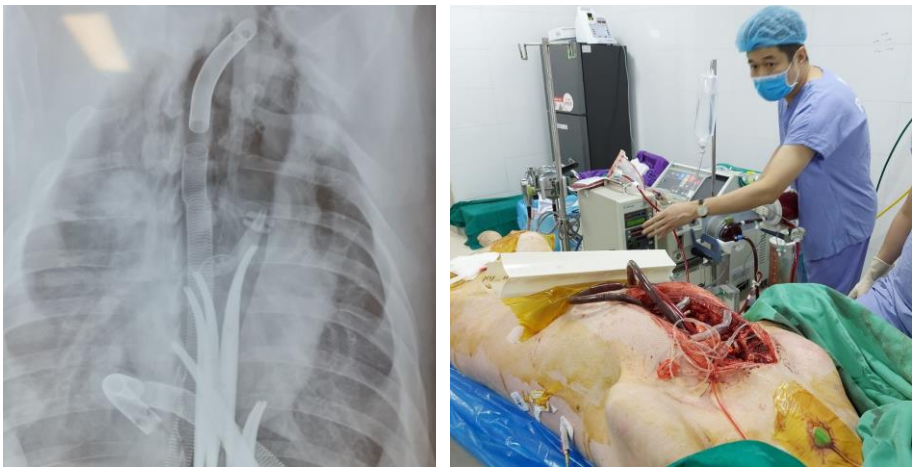


Figure 4. Chest radiograph after transplantation (left) and central ECMO support in the third case (right).

3.4 Coagulation and postoperative outcomes

Table 3. Findings at two hours and outcomes in individual recipients

Parameter	Case 1	Case 2	Case 3
Systolic / diastolic pressure (mmHg)	79 / 56	89 / 31	75 / 36
Heart rate (beats/min)	119	156	167
pH	7.30	7.29	7.19
PaO_2 (mmHg)	83	90	81
$PaCO_2$ (mmHg)	43	40	45
FiO_2	0.60	0.60	0.60
Calculated PaO_2/FiO_2 (mmHg)	138.3	150.0	135.0
EF (%)	70	73	85
Reported pulmonary artery pressure (mmHg)	25	32	40
Postoperative survival (min)	180	325	370

Note: Data represent individual values recorded at two hours postoperatively and final survival outcomes. Abbreviations: PaO_2, arterial partial pressure of oxygen; $PaCO_2$, arterial partial pressure of carbon dioxide; FiO_2, fraction of inspired oxygen; EF, left ventricular ejection fraction.

Coagulopathy occurred in all three cases. In case 2, bleeding through the left pleural drain was approximately 500 mL/h during the first two hours, necessitating re-exploration. Multiple bleeding sites were identified on the left-sided dissection surfaces. All three recipients died; mean postoperative survival was 291.7 ± 99.3 minutes, with a median of 325 minutes. Perioperative ACT profiles are shown in Figure 5.

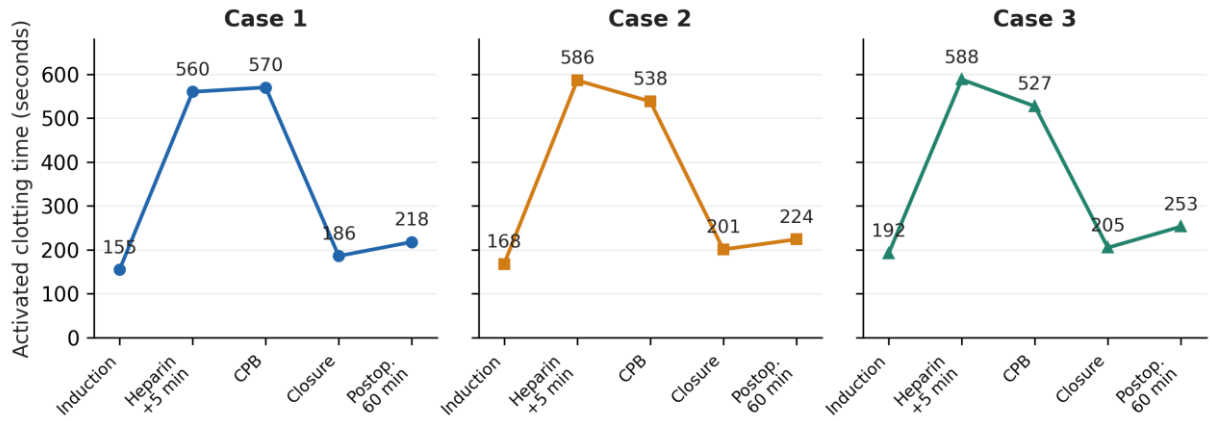


Figure 5. Activated clotting time (ACT) in each recipient at five perioperative stages. Labels show individual values in seconds. Mean ± SD across cases, in stage order: 171.7 ± 18.8; 578.0 ± 15.6; 545.0 ± 22.3; 197.3 ± 10.0; 231.7 ± 18.7 seconds. Stages are equally spaced for display and do not represent equal elapsed intervals. CPB, cardiopulmonary bypass

Packed red blood cell transfusion volumes were 2,950, 3,500, and 3,250 mL, respectively, with a mean of 3,233.3 ± 275.4 mL. Mean crystalloid and colloid volumes were 1,333.3 ± 288.7 mL and 666.7 ± 288.7 mL, respectively. These were the reported intraoperative volumes. Fluid balance and hourly total blood loss data were unavailable, preventing analysis of the relationships among fluid administration, coagulation, and graft function.

4. Discussion

4.1. Pioneering experience and multidisciplinary coordination

To our knowledge, 108 Military Central Hospital is the first institution in Vietnam to perform experimental en bloc heart–lung transplantation. A central contribution of this program was the establishment of five technical protocols linking animal preparation and logistics, anesthesia and resuscitation, cardiopulmonary bypass management, donor procurement and recipient implantation, and postoperative intensive care. These protocols provided a framework for coordination among the participating teams across the perioperative pathway. The three procedures allowed the teams to develop practical experience in integrating their respective tasks under the experimental conditions available at our institution.

The principal achievements of this study were the development of a coordinated set of protocols and the technical success of en bloc heart–lung transplantation in three recipient pigs. The return of cardiac activity, patent airways, and lung expansion demonstrate the feasibility of restoring anatomical continuity and early graft activity under the experimental conditions available at our institution. In a 2024 study of 319 adult heart–lung transplant recipients, Treffalls et al. reported one- and five-year survival rates of 84.0% and 59.5%, respectively [7]. These long-term clinical outcomes cannot be compared directly with the postoperative survival of only a few hours in our experimental series. They nevertheless indicate that further development of the model should address sustained graft function and postoperative survival.

Animal studies have different objectives and cannot be compared solely on the basis of follow-up duration. Qayumi et al. investigated ischemia-reperfusion injury in a swine model, with assessments at 30 minutes and two hours after transplantation [8]. A prespecified assessment time is not equivalent to the time of death. Accordingly, survival of 180-370 minutes in the present series should not be regarded as an outcome equivalent to that of a study in which assessment was intentionally completed after several hours.

Macris et al. described transplantation of the heart and one lung to preserve unilateral innervation and reduce blood loss [9]. That model differs from the present en bloc heart–lung model in the native lung retained, post-transplant physiology, and extent of dissection.

4.2. Technical aspects requiring standardization

In this series, performing the tracheal anastomosis first allowed completion of a deeply situated anastomosis while exposure remained favorable. Both caval anastomoses require accurate orientation, appropriate length, and avoidance of torsion. The graft must be assessed in its final position before tension on each anastomosis is evaluated. Preserving the connections between the heart and lungs limits the implantation procedure to the four anastomoses described above, but does not reduce the need for hemostasis across the extensive dissection surfaces.

The left azygos vein in swine has practical surgical implications. Crick et al. described its drainage into the coronary sinus system, together with differences in caval orientation compared with humans [3]. Our report likewise emphasizes inspection and secure closure of the divided left azygos vein stump. An occult bleeding site behind the graft may be difficult to access after reperfusion; inspection of this structure during graft preparation and before implantation may therefore help prevent bleeding.

In the third case, the superior vena caval anastomosis was performed after aortic unclamping. In principle, this modification may allow earlier reperfusion than waiting until all four anastomoses have been completed. However, the modification was used in only one case, there was no comparison group, and detailed procedural time logs were unavailable. Its effect therefore cannot be quantified, nor can a reduction in aortic cross-clamp time be attributed specifically to this change in sequence.

4.3. Critical care and limitations of functional assessment

Bleeding and coagulopathy were prominent problems in this series. Re-exploration in case 2 confirmed bleeding from the dissection surfaces; severe coagulopathy was reported in the other two cases. Prolonged CPB, extensive dissection, large transfusion volumes, and hypothermia are factors that warrant concurrent investigation.

ACT decreased after CPB but remained above baseline in each case at 60 minutes postoperatively. This finding warrants correlation with heparin and protamine doses, body temperature, and coagulation tests; it is insufficient to diagnose residual heparin activity. Management based on ACT alone may overlook other mechanisms of bleeding. Potential improvements include standardized assessment of hemostasis before and after reperfusion, hourly

recording of drain output, transfusion balance, and a coagulation testing strategy appropriate for the swine model.

At two hours, PaO_2/FiO_2 ratios were only 135–150 mmHg. Achieving a $PaO_2 \geq 75$ mmHg at an FiO_2 of 60% demonstrates the presence of gas exchange. However, primary lung graft dysfunction cannot be graded from this ratio alone without standardized imaging assessment, the required observation time points, and information on extracorporeal support. The ISHLT consensus emphasizes the combined assessment of oxygenation and imaging when evaluating primary lung graft dysfunction [10].

5. Conclusion

Three experimental en bloc heart–lung transplantations in swine were technically successful. Early graft activity met the study criteria.

Postoperative survival was approximately 3-6 hours, specifically 180, 325, and 370 minutes. These findings demonstrate technical success and initial graft activity. Extending survival will require further refinement of critical care and postoperative bleeding control.

To our knowledge, this is the first institutional experience of experimental en bloc heart–lung transplantation in Vietnam. The five technical protocols established a framework for coordinated work among animal preparation and logistics personnel, anesthesiologists, perfusionists, surgeons, and postoperative intensive care staff. This organizational and technical experience provides a foundation for further protocol refinement, multidisciplinary training, and progress toward clinical heart–lung transplantation in Vietnam.

Acknowledgements

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

Declaration of Generative AI and AI-Assisted Technologies

We declare that no artificial intelligence (AI) was used during the research process or in the writing of this manuscript.

Author Contributions

Tuan Anh Ngo contributed to the study conception and design, surgical procedures, data collection, data interpretation, and drafting of the manuscript. Van Vien Mai contributed to the study conception and design, surgical procedures, data collection, and revision and review of the manuscript. Vi Hai Ngo, Quoc Hung Nguyen and Huy Hieu Dao contributed to the surgical procedures and data collection. Tien Dong Nguyen and Quang Thai Tran contributed to anesthesia management, cardiopulmonary bypass, and data collection. Anh Tuan Hoang and Cong Hieu Dang contributed to the surgical procedures and perioperative data collection. Hoai Nam Ha contributed to the study conception and design, supervision, data interpretation, and revision and review of the manuscript. All authors read and approved the final manuscript.

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GHÉP KHỐI TIM PHỔI THỰC NGHIỆM TRÊN LỢN: KINH NGHIỆM BƯỚC ĐẦU TẠI VIỆT NAM

Ngô Tuấn Anh[1], Mai Văn Viện[1], Ngô Vi Hải[1], Nguyễn Quốc Hưng[1], Đào Huy Hiếu[1], Nguyễn Tiến Đông[1], Trần Quang Thái[1], Hoàng Anh Tuấn[1], Đặng Công Hiếu[1], Hà Hoài Nam[1*]

[1] Bệnh viện Trung ương Quân đội 108

TÓM TẮT

Mục tiêu: Mô tả kỹ thuật phẫu thuật và kết quả sớm của ghép khối tim phổi thực nghiệm trên lợn tại Bệnh viện Trung ương Quân đội 108. **Đối tượng và phương pháp:** Nghiên cứu thực nghiệm tiến cứu, mô tả loạt ba trường hợp ghép thực hiện năm 2021; mỗi cuộc mổ gồm: một lợn cho tạng, một lợn nhận và một lợn cho máu. Khối tim phổi được lấy, bảo quản lạnh và ghép qua đường mở dọc giữa xương ức, dưới tuần hoàn ngoài cơ thể (THNCT). Kỹ thuật gồm bốn miệng nối: khí quản, hai tĩnh mạch chủ và động mạch chủ. Phân tích mô tả thời gian phẫu thuật, huyết động, khí máu, siêu âm tim, đông máu và thời gian sống sau mổ. **Kết quả:** Xây dựng được năm quy trình kỹ thuật và hoàn thành ba ca ghép thành công về mặt kỹ thuật. Thời gian phẫu thuật trung bình 233,3 ± 50,3 phút; THNCT 160,3 ± 46,8 phút; kẹp động mạch chủ 81,0 ± 9,5 phút; bảo quản thiếu máu lạnh 17,0 ± 2,6 phút. Tim ghép đập lại ở cả ba ca; phân suất tống máu thất trái sau dừng THNCT đạt 70-85%. Ở giờ thứ hai, PaO_2 đạt 81-90 mmHg với FiO_2 0,60, tương ứng PaO_2/FiO_2 135-150 mmHg. Một ca phải mở ngực cầm máu lại; báo cáo ghi nhận chảy máu và rối loạn đông máu sau mổ. Cả ba lợn nhận tử vong sau 180, 325 và 370 phút. **Kết luận:** Theo hiểu biết của chúng tôi, Bệnh viện Trung ương Quân đội 108 là cơ sở đầu tiên tại Việt Nam thực hiện ghép khối tim phổi thực nghiệm. Nghiên cứu đã xây dựng năm quy trình kỹ thuật, tạo cơ sở phối hợp giữa bộ phận hậu cần và chuẩn bị động vật, gây mê hồi sức, tuần hoàn ngoài cơ thể, phẫu thuật và hồi sức sau mổ. Ba ca ghép thành công về mặt kỹ thuật, với thời gian sống sau mổ khoảng 3-6 giờ, cung cấp kinh nghiệm tổ chức và thực hành làm cơ sở tiếp tục phát triển kỹ thuật ghép khối tim phổi tại Việt Nam.

Từ khóa: ghép khối tim phổi; ghép tạng thực nghiệm; tuần hoàn ngoài cơ thể; kỹ thuật ghép hai tĩnh mạch chủ.