

The Cost of Heart Transplant in Iran: A Multicenter Analysis

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ABSTRACT

Background: Heart transplantation is an established treatment for end-stage heart failure patients, but its cost-effectiveness is under question.

Objective: This study aimed to assess the cost of heart transplantation in Iran as a developing country in Asia to contribute to future planning in the region.

Methods: This study was conducted in two phases. First, in a retrospective multicenter study, hospital data of heart transplant and hospitalization of three active heart transplant centers in Tehran, Iran, were reviewed from April 2013 to May 2015. Then pre-transplantation, transplantation, and one-year post-transplant costs were calculated according to the ABC (activity-based costing) method in 2016.

Results: Data were obtained for 120 patients, among which 95 (79.17%) were males with a mean (SD) age of 35.31±13.41 years. Mean (SD) hospital and ICU length of stay were 17.85±14.91 and 9.74±8.94 days, respectively. A significant correlation existed between the mean of hospital and ICU length of stay ($P<0.001$, $r: 0.754$). The mean heart transplant and hospitalization cost was 3445.47±1243.29 USD from 2013 to 2015. Using the activity-based costing method, the cost of pre-transplantation, transplantation, and one-year post-transplantation were extracted 6.5%, 73.5%, and 20%, respectively, with a total cost of 26232 USD.

Conclusion: Compared to other countries, the cost of heart transplantation in Iran is very low. Numerous reasons lead to this difference. Firstly, a heart transplantation surgery is performed in university-based hospitals and is supported by the government. On the other hand, a significant difference exists between personnel costs in Iran compared to other countries.

KEYWORDS: Heart transplantation; Activity-based costing; Heart failure; Heart surgery

INTRODUCTION

Heart failure (HF) is an issue with an increasing incidence that affects 23 million people in the world and more

than 5.8 million in the United States [1]. In Iran, the incidence of HF will increase to 3500 cases per 100,000 individuals in the future, and cardiovascular disorders such as HF are among the major causes of patient mortality and morbidity [2]. HF is associated with considerable morbidity and mortality, despite improvement in management. Over 2.4 million hospitalized patients have HF as a primary or secondary diagnosis, and practically 300,000

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deaths each year are instantly due to HF [3–5]. In the United States, management of HF has an immediate cost of over \$34 billion annually, most of which is due to hospitalization [6].

Heart transplantation is a recognized therapeutic modality for patients with end-stage heart failure [7]. Nevertheless, it is restricted by serious lack of donor organs, complications such as infection, rejection, allograft coronary arteriosclerosis as well as the requirement for long-term immunosuppressive therapy with its attendant effects. Although cardiac transplantation is regarded to be cost-effective in the long term [8], some research in recent decades focusing on in-hospital and procedure-related costs show that it is a costly treatment [9,10]; therefore, determining its costs has become important [11]. In Iran, the rate of brain death is high due to road accidents and trauma; however, rate of brain death donation is 14.34 per million population (PMP) (IRODaT 2019) [12]. The cost of medications plays a crucial role in heart transplantation cost evaluation. The most important categories of drugs heart transplantation are immunosuppressants, antibiotics, and antivirals regimens. Maintenance Immunosuppressive drugs include calcineurin inhibitors (such as the cyclosporine and tacrolimus) and inhibitors of purine synthesis (such as mycophenolate mofetil) and corticosteroid drugs (such as prednisolone) [13]. Valganciclovir has been known to inhibit cytomegalovirus (CMV) diseases in high-risk solid organ transplant (SOT) recipients [14]. Other medications include ranitidine, atorvastatin, calcium, alendronate sodium, and multivitamins. Without considering the exact cost of a transplantation operation, it is impossible to determine its cost effectiveness.

Although heart transplantation started in our country in 1993 [15], only the cost of kidney and lung transplant has been previously determined [16,17]. In this regard, no study exists on the cost and expenses of heart transplantation in Iran.

Regarding the importance of clear information about the cost of transplantation especial-

ly for government, insurance companies, and hospitals, we here aimed to report the cost of heart transplantation in Iran.

MATERIALS AND METHODS

This study was conducted in two phases. First in a retrospective multicenter study, hospital data of heart transplant and hospitalization of three active heart transplant centers in Tehran, Iran, were reviewed and analyzed from April 2013 to May 2015. Then, scientific transplant protocol of that three active heart transplantation centers was assessed via expert sessions, and pre-transplantation, transplantation, and one-year post-transplantation cost were calculated according to the ABC costing (activity-based costing) method in 2016.

Activity analysis within the ABC method evaluates resource consumption through activity identification [13]. Activity analysis provides information on what and how work is done, quality of the work, time to perform the work, the output of the work, patient and/or supplier relationships, and service relationships [14,18]. This method aims to calculate the indirect cost and thus total cost.

Categories constituting the total charges are defined as follows:

- 1) 30 days pre-transplant: These charges include all medical costs for the transplant patient incurred during the 30 days before the transplant hospital admission, including medical costs related to the transplant (visits, consultations, paramedical and laboratory, and radiologic evaluations).
- 2) Transplant: This covers facility charges for the transplant identified by the American Medical Association's Current Procedural Terminology (CPT) procedure codes (including surgery procedures, paraclinical, expenditure use and immunosuppressive, and other drugs provided during the hospital stay as well as room and board and ancillary services).
- 3) One-year post-transplant discharge: This

covers post-discharge facility and professional services, including any hospital readmissions. The services also include regular lab tests, regular outpatient visits, and evaluation and treatment of complications. Furthermore, all the outpatient drugs prescribed from discharge to one-year post-transplant discharge, including immunosuppressants and other needed drugs.

Ethical consideration

This study protocol was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences.

RESULTS

Data were obtained for 120 patients, including 95 (79.17%) males and 25 (20.83%) females with a mean age of 35.31 ± 13.41 years. Mean hospital and ICU length of stay were 17.85 ± 14.91 and 9.74 ± 8.94 days, respectively. A significant correlation existed between the mean of hospital and ICU length of stay ($P < 0.001$, $r: 0.754$).

The mean total cost of heart transplantation in Iran was 3445.47 ± 1243.29 USD (range: 1059.43 to 8510.55). This cost included surgery (66.02%), ICU (13.56%), paraclinical examination (9.16%), surgery unit (6.16%), expenditure tools (3.51%), rehabilitation (0.84%) and consultation (0.75%) (Tables 1 and 2).

All the medications consumed by the patients were estimated yearly. Table 3 shows the results. The total cost of heart transplantation in Iran was 26.232 USD, including pre-transplantation (6.5%), transplantation (73.5%), and one-year post-transplant charges (20%) (Tables 1 and 2). All the medications consumed by the patients were estimated yearly, and then the costs during the three years were evaluated. Table 3 shows the heart transplant cost in 2016.

DISCUSSION

Nowadays, cardiovascular diseases are among

the most important causes of mortality in the world, and according to the WHO prediction, they will change to the most important cause of mortality by 2020 [19,20]. According to previous studies, approximately 25-45% of mortalities in Iran are caused by cardiovascular diseases [21]. Among cardiovascular diseases, advanced heart failure is one of the most common cardiovascular problems in Iran (more than 3500 cases per 100000 people in Iran) [2]. Heart transplantation is accepted as the final therapeutic method for patients with end-stage heart failure [22]. According to exiting reports, approximately 500 heart transplantation surgeries are annually performed in Iran in seven active heart transplant centers up to 2015, while 400 patients were on the waiting list. Regarding the importance of this subject in the mortality of patients, for the first time, the cost of heart transplantation in Iran was evaluated in this study. Cost determination includes a total cost (of hospital admission), direct cost, indirect cost, fixed cost, and variable cost. Direct cost is defined as expenses directly related to patient care, whereas indirect cost represents expenses associated with hospital maintenance, administration, and utilities. Variable cost is affected by the patient volume, whereas fixed cost is not affected. We also divided total costs into subcategory components (e.g., surgery, ICU, paraclinical examination, surgery unit, expenditure tools, rehabilitation, and consultation) to determine the relative contribution of each item to the total resource consumption. Professional fees were included in the analysis. All the cost data reported herein are uncensored, implying that these data do not consider the financial impact of in-hospital death.

In the present study, 120 patients, including 25 women (20.83%) and 95 men (79.17%) with a mean age of 35.31 ± 13.41 were evaluated. These results were consistent with those obtained by Mandegar et al. in 2009, reporting the mean age of heart transplantation patients to be 29.30 ± 13.17 years [13]. In our study, the ratio of male to female was 3/8, which was parallel with the results of Aaronson et al. (1995) reporting this ratio as 3.24 and a correlation between gender and heart transplan-

Table 1: List of heart transplantation cost.

List	Mean ± S.D (USD)	Percent of the total cost
Surgery	2274.81 ± 837.55	66.02%
ICU	467.07 ± 549.03	13.56%
Paraclinical examination	315.56 ± 260.58	9.16%
Surgery unit	121.051 ± 125.00	6.16%
Expenditure tools	212.14 ± 447.23	3.51%
Rehabilitation	25.81 ± 26.60	0.84%
Consultation	29.00 ± 15.85	0.75%
Total	3445.47 ± 1243.29	100%

tation [23]. On the other hand, in our study, a direct and significant correlation existed between ICU residency and hospitalization time at the hospital; in this case, our results were consistent with previous studies showing the relationship between these two variables [24–26].

In the present study, the cost of a heart transplantation surgery is reported to be approximately 3845 USD in 2015 and 26232 USD in 2016. The major reason for this difference is related to sanctions and subsequent inflation and depreciation of currency, particularly affecting medical devices necessary for this procedure during that time.

In the case of cost, when the service code was defined in the relative value book, the service code was used for cost, and when it was not defined, the cost method was used. Due to the implementation of transplant services in the public hospitals as well as the location of the research, all costs were calculated for governmental centers.

The total cost of the pre-transplantation stage was 1694 USD, including the cost of evaluating and preparing the patient for transplant (visits, consultations, lab tests, paraclinical, and medicines). The largest part of the costs is related to the cost of paraclinical services. In the transplanting phase, the total patient cost was 19302 USD, for which the surgical cost was the highest, and paraclinical services had the lowest cost. The cost of linkage services for the patients during a one year follow-up is

5,267 USD with the highest cost being attributed to medications and the lowest cost being related to paraclinical services after surgery. The total cost of heart transplantation during one year is \$26,283 for which the highest cost was attributable to the costs of hospitalization for transplantation that was \$19302 (73.5%). It should be noted that the cost of postoperative care was \$5,267 (20%). (Table3). Thus, expenditures for the consumed drugs are 43%, healthcare services are 41%, equipment and devices 8%, and the expenditure for paraclinical services costs are 8%. Therefore, due to the high cost of transplant drugs and the effects of currency fluctuations on the cost of drugs and supplies, focusing on these can help to reduce the cost of transplantation.

The cost of heart transplantation in the United States has increased from 120,000 to 169,000 USD from 2005 to 2009 (27). The cost has been reported to be 76000 dollars in Virginia in 2001 (9). In addition, the cost of heart transplantation has been 44300 and 80000 dollars in the Netherlands and Spain, respectively (28,29). According to the 2014 Milliman Research Report on U.S. organ and tissue transplants, the cost for a heart transplant was \$1.2 million. The cost increased to \$1.66 million in the 2020 report [30]. Heart transplants are covered by health insurance in most cases in the United States, especially if the insurance plan is comprehensive. However, each insurance company may provide the coverage differently. In addition, the amount may be so considerable that the coverage provided by the health insurance may not be enough to

Table 2: Details of surgery and paraclinical examination cost.

	List	Mean ± S.D (USD)	Percent of the total cost
Surgery	Surgeon	757.72 ± 483.37	33.31%
	Surgeon assistant	182.91 ± 91.67	8.04%
	Anesthesia assistant	183.06 ± 97.15	8.05%
	Drug	454.42 ± 790.73	19.98%
	Expenditure tools	696.68 ± 262.76	30.62%
Paraclinical Examination	Echocardiography	41.95 ± 35.10	13.29%
	Laboratory tests	211.11 ± 191.15	66.91%
	Radiology	22.17 ± 54.21	7.02%
	CT scan	25.39 ± 13.77	8.03%
	Sonography	15.00 ± 7.07	4.75%

cover all the expenses.

Hence, the cost of heart transplantation is very lower in Iran in comparison to the mentioned countries. Various reasons can lead to this difference. Firstly, in Iran, all hospitals performing heart transplantation surgery are university-based hospitals and are supported by the government; On the other hand, a considerable difference exists between personnel costs in Iran compared to other countries at different stages of organ transplantation surgery (pre-operation, during operation and after operation). Furthermore, the studies have indicated that the costs of lung and kidney transplantation are significantly lower in Iran compared to other countries, and the noted reasons above might be the cause of this cost difference [14,15].

In the present study, the highest costs were related to the surgery team, expenditure tools, and medications, respectively. These results were parallel with those in the study by Ab-basi-Dezfouli et al. in (2009) evaluating the costs of lung transplantation in Iran [15], but they were not consistent with studies in other countries, where the highest costs were related to pre-transplant evaluation and testing, hospital charges, organ procurement, and follow-up care, respectively [9]. However, other costs also exist, which are related to heart transplants not covered by health insurance.

These may include food, lodging, and travel expenses of the patient and caregiver (to and from the hospital or transplant center), outpatient medications while the patient is recovering, visits to the unrelated transplant doctor, and home care.

The previous studies in other countries have reported the monthly mortality rate after heart transplantation surgery, to be 4% to 6.5%, and the yearly survival to be 85% [9,27,29], while according to the studies conducted in Iran, the yearly survival rate of patients is approximately 80%, and no significant difference exists in this aspect between Iran and other countries [31,32]. Furthermore, a 15-year study of heart transplantation surgery patients in Iran showed no significant difference in the survival rate of patients between Iran and other countries [13].

Heart transplantation is the most effective therapeutic approach for end stage cardiomyopathies and significantly decreases the mortality. In this regard, limitation of access to donor-organ and high costs of heart transplantation in many countries are among the limitations of this therapeutic method. Few studies have evaluated the cost-effectiveness of heart transplantation. Studies have indicated that in countries such as the United States, the Netherlands, and Spain, the costs of this operation are high and not economical compared to lung and kidney transplantations [9,28,29].

Table 3: Heart transplant cost during 2016 according to ABC method.

	List	Mean (USD)	Percent of the total cost
Pre-transplantation	Paraclinics	1145	4%
	Drugs	139	0.5%
	Medical services (visits, consults,...)	410	1.5%
	Total	1694	6.5%
Transplantation	Paraclinics	495	2%
	Drugs and Expenditure tools	8701	33%
	Medical services (visits, consults, ...)	10106	38.5%
	Total	19302	73.5%
Up to one-year post-transplant	Paraclinics	471	1.8%
	Drugs	4203	16%
	Medical services (visits, consults, ...)	562	2.1%
	Total	5236	20%
Total		26232	100%

Moreover, follow-up of the patients by phone call or Telemedicine modalities significantly decreased the expenses and mortality [33]. However, the results of our study showed that the cost of heart transplantation in Iran was acceptable; however, these results are not extendable to other countries due to differences in the health systems of various countries. One of the study limitations of the current study is that it was conducted in Tehran, the capital city of Iran.

In conclusion, the cost of heart transplantation in Iran is lower than that in many countries, while the one-year results are comparable with other countries. Transporting the donors from other cities to cities or hospitals where heart transplantation is to be performed is one of the major causes of the decreased cost, while the overall expenses in Iran are low [34].

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CONFLICTS OF INTEREST: None declared.

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REFERENCES

1. Bui AL, Horwich TB, Fonarow GC. Epidemiology and risk profile of heart failure. *Nat Rev Cardiol* 2011;**8**:30-41.
2. Bahrami M, Etemadifar S, Shahriari M, Farsani AK. Caregiver burden among Iranian heart failure family caregivers: A descriptive, exploratory, qualitative study. *Iran J Nurs Midwifery Res* 2014;**19**:56-63.
3. Lloyd-Jones D, Adams RJ, Brown TM, et al. Heart disease and stroke statistics--2010 update: a report from the American Heart Association. *Circulation* 2010;**121**:e46-e215.
4. Levy D, Kenchaiah S, Larson MG, et al. Long-term trends in the incidence of and survival with heart failure. *N Engl J Med* 2002;**347**:1397-1402.
5. Norton C, Georgiopoulou V V, Kalogeropoulos AP, et al. Epidemiology and cost of advanced heart failure. *Prog Cardiovasc Dis* 2011;**54**:78-5.
6. Fang J, Mensah GA, Croft JB, et al. Heart failure-related hospitalization in the U.S., 1979 to 2004. *J Am Coll Cardiol* 2008;**52**:428-34.

7. Chazal T, Varnous S, Guihaire J, *et al.* Sarcoidosis diagnosed on granulomas in the explanted heart after transplantation: Results of a French nationwide study. *Int J Cardiol* 2020;**307**:94-100.
8. Weiss MJ, Madsen JC, Rosengard BR, *et al.* Mechanisms of chronic rejection in cardiothoracic transplantation. *Front Biosci* 2008;**13**:2980-8.
9. Cope JT, Kaza AK, Reade CC, *et al.* A cost comparison of heart transplantation versus alternative operations for cardiomyopathy. *Ann Thorac Surg* 2001;**72**:1298-305.
10. Votapka T V, Swartz MT, Reedy JE, *et al.* Heart transplantation charges: status 1 versus status 2 patients. *J Heart Lung Transplant* 1995;**14**:366-72.
11. Rothman SM, Rothman DJ. The hidden cost of organ sale. *Am Soc Transpl Surg* 2006;**6**:1524-8.
12. International Registry on Organ Donation and Transplantation. Available from: <http://www.iro-dat.org/?p=database&c=IR#data>. (Accessed June 10, 2021)
13. Gujral S, Dongre K, Bhindare S, *et al.* Activity-based costing methodology as tool for costing in hematopathology laboratory. *Indian J Pathol Microbiol* 2010;**53**:68-74.
14. Brimson JA, Antos J. Activity-Based Management: For Service Industries, Government Entities, and Nonprofit Organizations: Wiley; 1994.
15. Mandegar M-H, Bagheri J, Chitsaz S, *et al.* Heart transplantation in iran; a comprehensive single-center review of 15-year performance. *Arch Iran Med* 2009;**12**:111-5.
16. Nourbala M-H, Einollahi B, Kardavani B, *et al.* The cost of kidney transplantation in Iran. *Transplant Proc* 2007;**39**:927-9.
17. Abbasi-Dezfouli A, Pojhan S, Behgam-Shadmeh M, *et al.* The cost of lung transplantation in Iran. *Ann Transplant* 2009;**14**:30-3.
18. Judith J. Baker. Activity-Based Costing and Activity-Based Management for Health Care. USA: Gaithersburg, Maryland; 2000.
19. Gaziano TA, Bitton A, Anand S, *et al.* Growing epidemic of coronary heart disease in low- and middle-income countries. *Curr Probl Cardiol* 2010;**35**:72-115.
20. Heidenreich PA, Trogon JG, Khavjou OA, *et al.* Forecasting the future of cardiovascular disease in the United States: a policy statement from the American Heart Association. *Circulation* 2011;**123**:933-44.
21. Talaei M, Sarrafzadegan N, Sadeghi M, *et al.* Incidence of cardiovascular diseases in an Iranian population: the Isfahan Cohort Study. *Arch Iran Med* 2013;**16**:138-44.
22. Perkel D, Czer LSC, Morrissey RP, *et al.* Heart transplantation for end-stage heart failure due to cardiac sarcoidosis. *Transplant Proc* 2013;**45**:2384-6.
23. Aaronson KD, Schwartz JS, Goin JE, *et al.* Sex differences in patient acceptance of cardiac transplant candidacy. *Circulation* 1995;**91**:2753-61.
24. Abelha FJ, Castro MA, Landeiro NM, *et al.* Mortality and length of stay in a surgical intensive care unit. *Rev Bras Anesthesiol* 2006;**56**:34-45.
25. Moitra VK, Guerra C, Linde-Zwirble WT, *et al.* Relationship Between ICU Length of Stay and Long-Term Mortality for Elderly ICU Survivors. *Crit Care Med* 2016;**44**:655-62.
26. Kramer AA, Zimmerman JE. The relationship between hospital and intensive care unit length of stay. *Crit Care Med* 2011;**39**:1015-22.
27. Mulloy DP, Bhamidipati CM, Stone ML, *et al.* Orthotopic heart transplant versus left ventricular assist device: a national comparison of cost and survival. *J Thorac Cardiovasc Surg* 2013;**145**:564-6.
28. Van Hout B, Bonsel G, Habbema D, *et al.* Heart transplantation in the Netherlands; costs, effects and scenarios. *J Health Econ* 1993;**12**:73-93.
29. Trilla A, Bertran M, Prat A, *et al.* Cost analysis of cardiac transplantation in a Spanish hospital. *Med Clin (Barc)* 2006;**126**:373-5.
30. Bentley TS, Hanson SG. Organ and tissue transplant cost estimates and discussion. Available from: <https://us.milliman.com/en/insight/2014-usorgan-and-tissue-transplant-cost-estimates-and-discussion>
31. Taheri M, Mandegar MH, Hossein Khan Z, *et al.* Twenty-two cases of simultaneous heart, liver, and kidney transplantation from brain dead patients. *Transplant Proc* 1998;**30**:773-4.
32. Ebong IA, Sayer G, Kim G, *et al.* Simultaneous heart, liver and kidney transplantation: A viable option for heart failure patients with multiorgan failure. *J Heart Lung Transplant* 2019;**38**:997-9.
33. Fadaizadeh L, Najafizadeh K, Shajareh E, *et al.* Home spirometry: Assessment of patient compliance and satisfaction and its impact on early diagnosis of pulmonary symptoms in post-lung transplantation patients. *J Telemed Telecare* 2016;**22**:127-31.
34. Najafizadeh K, Ghobadi O, Ghorbani F, *et al.* Transfer protocol of brain-dead patients to specialized donor management unit. *Transplantation* 2012;**94**:e6-8.