A REVIEW OF HEART TRANSPLANTS

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Heart transpolants

History: The world's first human-to-human heart transplant was performed by South African cardiac surgeon Christiaan Barnard utilizing the techniques developed by American surgeons Norman Shumway and Richard Lower. Patient Louis Washkansky received this transplant December 3, 1967, at the Groote Schuur Hospital in Cape Town, South Africa. Washkansky, however, died 18 days later from pneumonia.

How many heart transplants are done in India now?

Annually close to 750 organ donations happen in India, with **over 200 heart transplants**What is the success rate of heart transplant in India?

India being a major hub for health modalities across the globe, heart transplant in India has a success rate closer to **80-90%**.

Can you live 20 years with a heart transplant?

One fourth of all heart-transplant patients in our series survived >20 years with the same graft, and most enjoy independent lives despite significant comorbidities. Recipient age <45 years and idiopathic cardiomyopathy were associated with survival beyond 2 decades.

Can a human have a pig heart?

Doctors have transplanted the heart from a genetically modified pig into the chest of a man from Maryland in a last-ditch effort to save his life. The first-of-its-kind surgery is being hailed as a major step forward in the decades-long effort to successfully transplant animal organs into humans.

Heart transplants are performed when all other forms of medical treatment have failed.

Artificial hearts can be used temporarily until a human heart is available. If the whole heart cannot be transplanted, heart valves can still be donated.

When was first heart transplant in India?

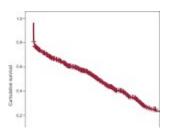
Jones and Kavita Sivaramakrishnan write: "On **February 17, 1968**, Bombay surgeon Prafulla Kumar Sen transplanted a human heart, becoming the fourth surgeon in the world to attempt the feat.

Even though the patient survived just three hours, the feat won Sen worldwide acclaim. Remembering Dr Prafulla K. Sen, who performed India's first human heart transplant...

What is the cost of heart in India?

Doctors generally suggest patients and their families to check their insurance plans for coverage of organ transplants. The average cost of a heart transplant can range anywhere

between 20 - 25 lakhs. This includes pre-transplant evaluation, the surgery itself and post-transplant recovery period.



Which hospital is the best for heart transplant in India?

Figure 1 Heart Transplant
Survival Rate

Apollo Hospitals, Chennai has successfully performed several Heart transplants, Lung transplants, Heart and Double Lung transplants and Heart Lung and Kidney transplantations and is regarded as the best heart transplant surgery hospital in India.

What is the age limit for heart transplant? Hospitals have traditionally set **65** as the upper limit for heart transplant. But older patients increasingly are getting them, and there is no absolute cut-off age.

Can you live 30 years after heart transplant? At almost 30 years, he's lived far longer than most heart transplant recipients. **The current world record**: 33 years. "James is an incredible example of someone who's been given the gift of life for 29 years after heart transplant," says Dr. Frank.

Is heart transplant possible in India?

India's heart transplantation programme is the number one programme in South Asia with an average heart transplantation rate of **0.2 per million population** (pmp) versus the global average of 1.06 pmp (2016-2018). The deceased donation rate was 0.67 pmp in India in 2018.

Who is the longest heart transplant survivor? Meet Minnesota's own **Cheri Lemmer**, the longest-surviving heart transplant recipient in the world.

What animal has 4 hearts?

Considered a primitive animal, the hagfish looks like an eel but is considered a fish. It is equipped with four hearts and between five and 15 pairs of gills that help oxygenate its blood. One of its four hearts, a branchial heart, pumps blood to the entire body while the other three are considered accessory pumps.

Which animal heart is closest to human?

Pig hearts are anatomically similar to human hearts but, understandably, not identical. It's not ideal, compared to swapping in a human donor heart. But it is possible to plumb them in and get them working.

What is the hardest organ to transplant? Of all the organs transplanted **the lungs** are the most difficult.

Who is the first organ donor in India?

The donor was **Karl Brauer**, an 11-year old boy who had iron metal bodies lodged in his eyes. The recipient was Alois Glogar, a 45-year-old day labourer whose corneas were damaged. His one eye had a clear vision after the transplant but other one had complications. India's first cornea transplant happened in 1948.

Heart transplants in India:

There is an original research article by faculties and students of AIIMS, Delhi: by cardiothoracis surgery and pathgology.

"Heart transplant in India: Lessons learned" Introduction: Heart transplants in India:

Heart transplant remains the gold standard for the treatment of end-stage heart failure. The first successful heart transplant in India was done at the All India Institute of Medical Sciences (AIIMS), New Delhi on August 3, 1994. The patient survived for 14 years. The longest surviving recipient at this institute is currently 16-year post heart transplant. Two decades later, the transplant program has not progressed in the way it should have progressed

India.
In the recent past, there has been an

in



Figure 2 Hagfish

increase in the number of centers performing heart transplant. A new organization by the name of National Organ and Tissue Transplantation Organization (NOTTO) has also come into existence which not only records, regulates, and facilitates organ transplantation but also creates awareness by its various

outreach programs and activities. This has led to an increase in the number of heart donors in the past 3 years. Although the increase in percentage may not seem very significant, it is a positive trend. At our institute also, there has been a surge in the number of heart transplant surgeries in the past 3 years (31 transplants in 1994–2014 and 25 in 2014–2017). With the increase in volumes, we have learned a number of lessons and fine-tuned our protocols for India.

Survival after heart transplants in India:

Most common cause of transplant was dilated cardiomyopathy (72%).

From 2014 to 2017, the volume of transplants increased as many centers all over India have started heart transplants with an increase in the transplant numbers, there was also an increase and then a decrease in the rate of complications as the surveillance and treatment protocols were revised.

"Contraindications"

Some patients are less suitable for a heart transplant, especially if they suffer from other circulatory conditions related to their heart condition. The following conditions in a patient increase the chances of complications.

Absolute contraindications:

- Irreversible kidney, lung, or liver disease.
- Active cancer if it is likely to impact the survival of the patient.
- Life-threatening diseases unrelated to the cause of heart failure, including acute infection or systemic disease such as systemic lupus erythematosus, sarcoidosis, or amyloidosis.
- Vascular disease of the neck and leg arteries.
- High pulmonary vascular resistance over 5 or 6 Wood units.

Survival longer than 20 years...

Departamento de Cardiología, Hospital Puerta de Hierro, Majadahonda, Madrid, Spain have studied this as a research project. The brief details are as below

Results

A total of 39 patients who survived 20 years (26% of patients transplanted before 1992) were compared to 90 recipients from the same period who died between 1 and 20 years posttransplantation. Major complications were hypertension, renal dysfunction, infections, and cancer. After a mean follow-up of 30 months, 6 survivors had died, yielding a mortality rate of 6% per year (vs 2.5%-3% in years 1-19). Causes of mortality were infection (50%), malignancy (33%), and allograft vasculopathy (17%). Longterm survivors were younger and leaner, and had nonischemic cardiomyopathy and lower ischemic time. Logistic regression identified recipient age <45 years (odds ratio=3.9; 95% confidence interval, 1.6-9.7; P=.002) and idiopathic cardiomyopathy (odds ratio=3; 95% confidence interval, 1.4-7.8; P=.012) independent predictors for 20-year survival.

Conclusions

One fourth of all heart-transplant patients in our series survived >20 years with the same graft, and most enjoy independent lives despite significant comorbidities. Recipient age <45 years and idiopathic cardiomyopathy were associated with survival beyond 2 decades. These data may help decide donor allocation.

The number of heart-transplant recipients exceeding 20 years of follow-up is steadily increasing. However, little is known about their functional status, co-morbidities, and mortality. Identifying the predictors of prolonged survival could guide the selection of candidates for the low number of available donors.

Functional status, morbidities, and mortality of heart-transplant patients between 1984 and 1992 were analyzed. To identify predictors of 20-year survival, a logistic regression model was constructed using the covariates associated with survival in the univariate analysis.

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A US man has become the first person in the world to get a heart transplant from a genetically-modified pig.

David Bennett, 57, is doing well three days after the experimental seven-hour procedure in Baltimore, doctors say.

The transplant was considered the last hope of saving Mr Bennett's life, though it is not yet clear what his long-term chances of survival are. "It was either die or do this transplant," Mr Bennett explained a day before the surgery.

"I know it's a shot in the dark, but it's my last choice," he said.

Doctors at the University of Maryland Medical Center were granted a special dispensation by the US medical regulator to carry out the procedure, on the basis that Mr Bennett - who has terminal heart disease - would otherwise have died.

• Three ethical issues around pig heart transplants

He had been deemed ineligible for a human transplant, a decision that is often taken by doctors when the patient is in very poor health. The pig used in the transplant had been genetically modified to knock out several genes that would have led to the organ being rejected by Mr Bennett's body, the AFP news agency reports.

For the medical team who carried out the transplant, it marks the culmination of years of research and could change lives around the world.

Surgeon Bartley Griffith said the surgery would bring the world "one step closer to solving the organ shortage crisis". Currently 17 people die every day in the US waiting for a transplant, with more than 100,000 reportedly on the waiting list.

Dr Christine Lau, chair of the Department of Surgery at the University of Maryland School Of Medicine, was in the operating theatre during the surgery.

"He's at more of a risk because we require more immunosuppressant, slightly different than we would normally do in a human-to-human transplant. How well the patient does from now is, you know, it's never been done before so we really don't know," she told the BBC.

"People die all the time on the waiting list, waiting for organs. If we could use genetically engineered pig organs they'd never have to wait, they could basically get an organ as they needed it.

"Plus, we wouldn't have to fly all over the country at night-time to recover organs to put them into recipients," she added.

The possibility of using animal organs for socalled xenotransplantation to meet the demand has long been considered, and <u>using pig heart</u> valves is already common.

In October 2021, surgeons in New York announced that they had successfully transplanted a pig's kidney into a person. At the time, the operation was the most advanced experiment in the field so far.

However, the recipient on that occasion was brain dead with no hope of recovery.

A glimmer of hope alongside huge risks

This watershed moment provides hope of a solution to the chronic shortage of donor human organs. But there is still a long way to go to determine whether giving people animal organs is the way forward. Pig hearts are anatomically similar to human hearts but, understandably, not identical. It's not ideal, compared to swapping in a human donor heart. But it is possible to plumb them in and get them working.

The bigger issue is organ rejection. These pigs are bred to lack genes that can cause rejection. They are cloned with certain genes "knocked out" and reared until they reach an age where their organs are big enough to be harvested for transplantation.

It is too soon to know how Mr Bennett will fare with his pig heart. His doctors were clear that the surgery was a gamble. The risks are huge, but so are the potential gains.

Mr Bennett, however, is hoping his transplant will allow him to continue with his life. He was bedridden for six weeks leading up to the surgery, and attached to a machine which kept him alive after he was diagnosed with terminal heart disease.

Media caption,

Watch: Muhammad Mohiuddin from the University of Maryland calls the transplant a "game-changer"

"I look forward to getting out of bed after I recover," he said last week.

On Monday, Mr Bennett was reported to be breathing on his own while being carefully monitored.

But exactly what will happen next is unclear.

Mr Griffith said they were proceeding cautiously and carefully monitoring Mr Bennett, while his son David Bennett Jr told the Associated Press that the family were "in the unknown at this point".

But he added: "He realizes the magnitude of what was done and he really realizes the importance of it."

"We've never done this in a human and I like to think that we, we have given him a better option than what continuing his therapy would have been," Mr Griffith said. "But whether [he will live for] a day, week, month, year, I don't know."

David Bennett (right) is said to be doing well



Figure 3 IMAGE SOURCE, UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE

after the surgery.

Prof Savulescu says before any surgery, the procedure must have undergone "very rigorous tissue and non-human animal testing" to make sure it's safe.

Mr Bennett's transplant was not performed as part of a clinical trial, as is usually required for experimental treatments. And the drugs he was given have not yet been tested for use in non-human primates.

But Dr Christine Lau from the University of Maryland School of Medicine, who was involved in planning Mr Bennett's procedure, said no corners were cut when preparing for the operation.

"We've done this for decades in the lab, in primates, trying to get to the point where we think it is safe to offer this to a human recipient," she told the BBC.

Animal rights

Mr Bennett's treatment has also re-sparked a debate over the use of pigs for human transplants, which many animal rights groups oppose.

One of them, People for the Ethical Treatment of Animals (PETA) has condemned Mr Bennett's

pig heart transplant as "unethical, dangerous, and a tremendous waste of resources".

"Animals aren't tool-sheds to be raided but complex, intelligent beings," PETA said.

Campaigners say it is wrong to modify the genes of animals to make them more like humans. Scientists altered 10 genes in the pig whose heart was used for Mr Bennett's transplant so it would not be rejected by his body.

The pig had its heart removed on the morning of the operation.

A spokesperson for Animal Aid, a UK-based animal rights group, told the BBC it was opposed to modifying animal genes or xenotransplants "in any circumstances".

"Animals have a right to live their lives, without being genetically manipulated with all the pain and trauma this entails, only to be killed and their organs harvested," the organisation said. Some campaigners have concerns regarding the unknown long-term effects of genetic modification on the pig's health.

• GM pigs take step to being organ donors

Dr Katrien Devolder, a fellow in bioethics at Oxford University, says we should only use gene-edited pigs for organs if we can "ensure they do not suffer unnecessary harm".

Genetically engineering pigs as organ donors

Adding and removing genes
with gene-editing technology
creates genetically-altered
pig cells



These are used to make pig embryos



The genetically-engineered pigs are raised in a controlled, bio-sealed environment



The organ is removed from adult pig and transplanted into patient



Patient must still take immunosuppressant drugs, to prevent their body rejecting the new organ



Source: University of Maryland School of Medicine, NYU Langone Health

"Using pigs to produce meat is much more problematic than using them to save lives, but of course that's no reason to ignore animal welfare here as well," she says.

Another quandary could emerge around those whose faiths might mean it is tricky for them to receive an animal organ.

Pigs are chosen as the relevant organs are a similar size to humans' - and because pigs are relatively easy to breed and raise in captivity. But how does this choice affect Jewish or Muslim patients, whose religions have strict rules on the animal?

Although Jewish law forbids Jews from raising or eating pigs, receiving a pig heart is "not in any way a violation of the Jewish dietary laws", says Dr Moshe Freedman, a senior London rabbi who sits on the UK Health Department's Moral and Ethical Advisory Group (MEAG).

"Since the primary concern in Jewish law is the preservation of human life, a Jewish patient would be obligated to accept a transplant from an animal if this offered the greatest chance of



Figure 4 IMAGE SOURCE, GETTY IMAGES

survival and the best quality of life in the future," Rabbi Freedman told the BBC.

No conflict of Interest

References:

- Airan B, Singh SP, Seth S, Hote MP, Sahu MK, Rajashekar P, Devagourou V, Das S, Parakh N, Ray R, Arava S. Heart transplant in India: Lessons learned. J Pract Cardiovasc Sci 2017;3:94-9
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Javier Segovia, Manuel Gómez-Bueno, Dolores García-Cosío, Evaristo Castedo, Santiago Serrano, Raúl Burgos, Carlos García Montero, Juan Ugarte, Paloma Martínez Cabeza, Luis Alonso-Pulpón

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- 3. New Scientist: How a pig heart was transplanted into a human for the first time The first transplant of a pig heart g? enetically modified for acceptance into human bodies raises hopes for a new solution to donor organ shortages.
- 4. Kilic A, Emani S, Sai-Sudhakar CB, Higgins RS, Whitson BA, et al. (2014). "Donor selection in heart transplantation". Journal of Thoracic Disease. 6 (8): 1097–1104. doi:10.3978/j.issn.2072-1439.2014.03.23. PMC 4133543. PMID 2513 2976.
- Cook JA, Shah KB, Quader MA, et al. (2015). "The total artificial heart". Journal of Thoracic Disease. 7 (12): 2172–80. doi:10.3978/j.issn.2072-1439.2015.10.70. PMC 4703693. PMID 2679 3338.
- Till Lehmann (director) (2007). The Heart-Makers: The Future of Transplant Medicine (documentary film). Germany: LOOKS film and television.
- 7. Burch M.; Aurora P. (2004). "Current status of paediatric heart, lung, and heart-lung transplantation". Archives of Disease in Childhood. **89** (4): 386–89. doi:10.1136/adc.2002.017186. PMC 171 9883. PMID 15033856.
- 8. May Transplant the Human Heart (.PDF), The New York Times, January 2, 1908.
- 9. Hardy James D.; Chavez Carlos M.; Kurrus Fred D.; Neely William A.; Eraslan Sadan; Turner M. Don; Fabian Leonard W.; Labecki Thaddeus D. (1964). "Heart Transplantation in Man". JAMA. **188** (13). doi:10.1001/ja
- 10. BBC world News, London U.K.