Benefit Definition: General Principles on Solid Organ Transplants

07 March 2012

Version 1.0

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1 Background

Organ transplant is a prescribed minimum benefit for conditions that require transplant. Organ transplant in South Africa has been slower than many countries and has actually declined over the last few years (1).

Due to lack of cadaver donors, the rate of live donor transplant is increasing worldwide, in Germany 40% of all kidney transplant are from live donors(2). In South Africa 33% of kidneys transplanted are from living donors. Although the incidence of living liver donors is increasing worldwide, living donor transplants in South Africa are relatively rare due to availability of the cadaver livers and limited skills in living donor liver transplant.

The total benefits (quality of life, survival, psychological and social well being) of paired donor recipient pair must always outweigh the risk (medical, social and psychological co-morbidities) of donor-recipient pair (3) (4). In South Africa, the minister must approve all non-related live donor transplant to ensure that donation of organs is fair.

National Health Act of 2003 regulate donation of organs, therefore this benefit definition must be read together with this Act and the conditions stated in act are considered prescribed minimum benefits.

2 Benefit definition for organ transplant

Benefits for organ transplant should include the following:

i. Evaluation of recipient and living or cadaver donor
ii. In-Hospital care of both the donor and recipient
iii. Post operative care and follow-up of the recipient and living donor

3 Evaluation and inclusion criteria

3.1 Evaluation

3.1.1 Recipient evaluation

The primary objective in evaluating a potential candidate for organ transplant is to determine the severity of the disease and assess if the client meets suitable entry criteria for organ transplant. The objective assessments will include a comprehensive psychosocial and medical assessments; which includes laboratory and radiological evaluation. The goal of this evaluation is 4-fold.

a) it must establish a diagnosis of end stage organ failure;

b) it must exclude any absolute or relative contraindication to the proposed procedure;
c) it must assess the suitability and degree of illness of each patient to better allocate resources and optimise survival.

d) It must assess whether the patient is psychologically ready to take transplant and assess the factors that may affect compliance

It is recommended that eligibility for a transplant be conducted in a multidisciplinary setting by an experienced team. A multidisciplinary work-up will include the services of physicians, surgeons, anaesthetist, nurses, psychologists, and others. A multidisciplinary assessment ensures that only suitable candidates are enrolled, improves the transplant outcomes, and therefore offers value for money.

Care for candidates with end stage organ disease who do not meet the criteria for organ transplant is a prescribed minimum benefit.

3.1.2 Live donor evaluation

This multiphase process may start with family submitting names of living donors. To prevent unnecessary expenses, donor evaluation should be done in tandem and not simultaneously. There is incomplete data to indicate the exact number of patients who need to be screened for compatibility. Expert opinion from Charlotte Maxeke hospital indicates that 2-3 evaluations are necessary. (5)

The evaluation of donor includes 3 phases: psychological assessment, compatibility assessment and medical assessment.

Phase 1: Psychosocial assessment

A preliminary psychosocial assessment is required to determine the desire to donate, to provide the patients with risks associated with procedure and all information required giving informed consent. A grace period of around 3 months allowed for the donor to consider. The full social assessment must be conducted to evaluate possible social and financial risks that the donor may face after donation (3).

Phase 2: Compatibility assessment

After the donor has agreed to voluntary donate an organ, the second phase is to determine if they are compatible with the recipient. Blood type should be determined before proceeding with medical assessment and other compatibility tests such as cross matching and tissue typing.

Phase 3: Medical suitability

This includes a consultation with a physician to screen and exclude medical conditions. Medical assessment should be conducted by a physician who is not involved in the care of a recipient for independent opinion. The main aim of the assessment is to assess the health of the donor, predict the risk associated with surgery itself and organ donation, exclude infections and malignancy and assess the transplantability of the organ being donated. The assessment includes consultation with various clinicians, diagnostic and pathology tests. (The specific diagnostic and pathological tests will be discussed under specific organ donation).
Medical assessment includes compatibility assessment which include blood grouping and compatibility assessment. The radiological and blood tests may be included.

3.1.3 Evaluation of the cadaver or brain dead donor
The evaluation of the cadaver and brain dead donor will include the blood tests to exclude infections and determine compatibility. Certain diagnostic tests (X-ray, MRI, or sonar) might be required to assess the condition of organ being harvested for transplants. During evaluation, care of brain death patients can extend to few hours after certified brain death. The main aim in care of brain death donor before harvesting of organs is to maintain normal haemodynamic and laboratory parameters.

3.2 Inclusion Criteria

3.2.1 Inclusion criteria for recipient
General principles of inclusion are discussed here. Specific inclusions are stated under the specific organ transplant definitions.

i. **Age of patients for transplant**: Age is not a criterion for listing but medical fitness is. Older patients (>55y) should only receive an older donor’s kidney (as in the Expanded Criteria Kidney transplant in Western Cape). For older (>55y) recipients life expectancy with a transplant should be at least 5 years in order to be considered for transplantation. (1)

ii. **HIV infections**: Patients with HIV should be considered for transplant, however patients should first be started on anti-retroviral treatment for at least 6 months and viral load should be less than 400 copies/ml. Patients should be adherent on antiretroviral. HIV positive patients may receive an organ donated from an HIV infected donor. (1)

iii. **Tuberculosis**: Patients with TB must first be treated with anti-TB drugs, complete course of treatment and declared cured (either sputum/ X-ray or clinical findings for extra-pulmonary TB)

iv. **Alcohol abuse and alcoholism**: Patients with alcoholism may be facing challenges that may affect the adherence to post-transplant treatment. Exclusion of alcoholics should be based on psychosocial assessment and the clinical risk factors that may threaten the success of the transplant. Similarly, exclusion of recovering alcoholics should be a based on the outcome of psychosocial evaluation and decision made by the multidisciplinary transplant team.

v. **Malignancy**: Patients with malignancies are not illegible for transplant unless the cancer is curable, cured or in remission. See Annexure A for guidelines in malignancy remission

vi. **Non-compliance to treatment**: A history of non-compliance alone should not be used to exclude patients on treatment. Patients need to be counselled to understand the requirements of treatment adherence, and support must be offered. Non-adherence is caused by multiple factors and in the instance of non-adherence, a rigorous an independent psychosocial assessment by the transplant and care team is required.

vii. **Debilitating diseases**: Patients who already suffer from a disease with poor prognosis should not be offered transplant. These patients are not discriminated based on their illness but on availability of resources and overall survival rate. Diseases with poor
prognosis may reduce their overall survival rate, therefore rendering transplant in this
group of patients not cost-effective.

viii. **Obesity:** A body mass index (BMI) > 35 may increase postoperative complications,
obesity is a relative exclusion, and patients cannot be excluded on transplant based on
obesity alone. A full risk assessment is required by the transplant team.

ix. **Immunisation:** All transplant recipients must provide proof of receiving SA childhood
immunisation; otherwise, they should receive immunisation at least 6 weeks before
transplant. Patient should receive annual immunisations such as flu vaccination as
they are immune-compromised.

x. **Approval of the transplant by multidisciplinary team:** Transplants depends on
availability resources and equitability distribution of organs. The decision to carry out
transplant must always be made by a multidisciplinary team experienced in
transplants.

xi. **South African citizenship:** All transplants in non-citizens of South Africa should be
approved by the minister first.

### 3.2.2 Inclusion criteria for living donors

#### 3.2.2.1 Voluntary living donors

a. The donor must be able to give informed consent: health care workers should enable the
participant by presenting the risks and benefits associated with donation of an organ

b. The donor must understand the donation procedure, benefits and risks associated with the
procedure

c. The donor must be of legal age and competent to give consent

d. The decision to donate must be autonomous and free of financial or social cohesion

#### 3.2.2.2 Medical eligibility

a. Living donor must be above 18 years old and not suffer from any mental health illness as per
section 58 of National Health Act and DSM IV criteria

b. They must have a BMI of 18-35 kg/m²

c. Blood group must be compatible

d. No significant anaesthetic risk

e. No active bacterial, viral, fungal or parasitic infections

f. Patients should not be pregnant

g. No diseases associated with organ being donated.

h. No cardiovascular or neurological diseases

i. No malignancy in the last five years

j. Must meet all the criteria as the National Health Act

#### 3.2.2.3 Psychological eligibility

a. Donors must be emotionally stable, without any mental health illness
b. Donors must be emotionally or genetically related to a recipient unless the donor is a good Samaritan donor or paired donor. Good Samaritan (unrelated) donors are subject to the approval of the Minister.

c. A past history of substance/or alcohol misuse by itself is not an exclusion by itself. The multidisciplinary team should assess the member an exclude problematic substance/ alcohol misuse. If patients suffer from substance or alcohol misuse, then they are not mentally competent o give consent.

3.2.3 **Inclusion criteria for cadaver and brain dead donors**

i. Age: Up to 70 years old or younger, premature babies < 500mg must be excluded

ii. Brain death declaration by neuro-surgeons according to government definition of brain death

iii. No malignancies or previous malignancies with evident metastasis

iv. No haematological malignancies or aplastic anaemia

v. No multiple organ failure

vi. The following active infections may not be present:

   a) **Bacterial infection**
      
      - Tuberculosis
      - Gangrenous bowel or perforated bowel and/or intra-abdominal sepsis

   b) **Viral infections**
      
      - HIV infection by serologic or molecular detection: however HIV donors can be considered for suitable HIV recipients
      - Rabies
      - Reactive Hepatitis B Surface Antigen
      - Retroviral infections including HTLV I/II
      - Viral Encephalitis or Meningitis
      - Active Herpes simplex, varicella zoster, or cytomegalovirus vireamia or pneumonia
      - Acute Epstein Barr Virus (mononucleosis)
      - West Nile Virus infection
      - SARS

   c) **Fungal infections**
      
      Active infection with Cryptococcus, Aspergillus, Histoplasma, Coccidioides Active candidemia or invasive yeast infection

   d) **Parasites**
      
      1. Active infection with Trypanosoma cruzi (Chagas’)
      2. Leishmania, Strongyloides, or Malaria (Plasmodium spp.)

   e) **Prion: Creutzfeldt-Jacob disease**

4 **Intra-operative care and in-hospital care**

Transplant can be offered only in accredited facilities in accordance with the National Health Act. Depending on the procedure; average length of hospital stay for donors is 7 days on average (with a range of 2-28 days), and hospital stay amongst recipients average 11 (± 7) days. (Range: 2-28 days).
Care must include all surgery, in-hospital and post-operative recovery in hospital. This should include all diagnostic tests, pathological tests, drugs and all material required to care for the patient. The health care providers required to render the services include all the clinicians and allied health workers (physiotherapist and occupational therapist).

5 Post-operative care and follow-up

5.1 Care of donors
The median morbidity rate amongst the living liver donors is 16% (4) and amongst living kidney patients is 10% (6) in experienced settings. Complications include medical complications, pain as well as psychological complications. (2) (6) (7). The long term complications of nephrectomy include chronic kidney disease as well as cardiovascular disease. (8) Post operative care of donors includes medical follow-up to monitor the functioning related to the specific organ that was donated, to monitor the healing process, and to manage all complications associated with donation, which include pain management. Donors must have access to physiotherapy and occupational therapy during recovery. Care of these patients includes all pathological tests, diagnostic tests, and consultations. Care must be extended until the donor has recovered completely from surgery and includes management of all complications as a result of surgery. The specific follow-up of a donor are discussed specifically under the specific organ transplant.

5.2 Care of recipients
Post-operative care includes numerous visits to the transplant team, which may average 14 visits in the first year post-operatively. This reduces to quarterly from the second year onwards depending on the type of transplant. The aim of the follow-up immediately post-operatively is to determine post-operative complications, evaluate the healing process, and tolerance of immunosuppressive drugs. In the long-term, the follow-up aims at to establish the functionality of the transplanted organ and the continuous evaluation of the long term effects of immunotherapy.

Care of recipients should include the following:

i. Consultations with relevant clinician including psychotherapy and other professionals in a transplant team
ii. Rehabilitation by physiotherapist or occupational therapist
iii. Diagnostic imaging required to access functionality of the organ
iv. Pathological tests required to monitor functioning of the organ and potential complication due to transplant (this include rest to screen or diagnose complications secondary to transplant drugs)
v. Life-time immunosuppressive drugs and drugs to alleviate or prevent side effects associated with immunosuppressive therapy. Examples include immunisations (flu, pneumococcal), immune boosting drugs, prophylactic treatment (e.g. Co-trimoxazole). Details are discussed in the specific organ transplant benefits
vi. Analgesia
6 Principles around funding of donor organs

6.1 Recipients
Organ donation is a PMB, all costs associated with evaluation, surgery, in-hospital care, and lifetime follow-up should be paid in full according to Regulation 8 of Medical Scheme Act 131 of 1998.

6.2 Living donor
South Africa’s experience on the long term follow-up of donors is limited; whilst state sector may cover uninsured recipients and beneficiaries, complications after donation may increase the health insurance risk on medical schemes.

The medical scheme of the recipient shall be liable to fund for screening, harvesting of organs and post-operative care. Living donors must be protected against out-of-pockets payment related to organ donation. First world countries have reported the dilemma for long-term follow-up of complications in donors especially when the recipient had died or is no longer part of the medical scheme (3). Donors may experience complications related with donation after an apparent successful recovery and event free period. (E.g. renal disease in living kidney donors). Donors must be followed up for lifetime as long as the beneficiary is a member of the scheme. This follow-up is limited to periodic screening of diseases associated with transplant, however does not include management of complications detected.

Due to complexities of belonging to 2 medical schemes, it will be the responsibility of the donor’s medical scheme to continue with long term follow-up which include screening of diseases associated with organ harvested. This should be funded as a prescribed minimum benefit. Therefore, the recipient’s scheme and the donor should inform the donor’s scheme prior to proceeding with transplant and the donor’s scheme.

The benefits of harvesting organs include all operations, hospital stay, and the cost of the preparatory investigations.

6.3 Brain dead/cadaver donor
Care of brain dead patients can extend long after certified brain death. The main aim in brain death donors is to maintain haemodynamic and metabolic parameters. Managing the organ donor following determination of brain death is multifaceted and involves a comprehensive system for medical care of the donor, which may include administering appropriate medications to maintain basic body and organ functions and the monitoring of physiologic values like oxygen, hormone, and electrolyte levels in the blood (9). The cost of maintaining the body on ventilator post brain death, harvesting of the organs shall be equally distributed amongst the recipients. The funders (medical schemes or government in state patients) of the recipients should equally the share of the costs. The medical schemes may enquire about distribution of organs too ensure that they are appropriately billed. Post-harvesting; the funders of each recipient should cover the costs associated with maintenance and transportation of the organs allocated to the recipient. Currently there is no solid organ bank in South Africa; therefore, costs associated with storage of the solid organs will not applicable. The recipient’s medically scheme shall pay for the costs directly associated with the transportation and preservation of specific organ for the beneficiary.
## Annexure 1: Minimum transplant recommendations for malignancies.

<table>
<thead>
<tr>
<th>Type of Cancer</th>
<th>Recommendation (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer</td>
<td>&gt; 5 (&gt; 2 for early disease)</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>&gt; 5 (&gt; 2 for Dukes Stage A or B1)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>&gt; 5 (&gt; 2 melanoma in situ)</td>
</tr>
<tr>
<td>Uterine cervical cancer</td>
<td>&gt; 2 (&gt; 5 for more advanced cervical)</td>
</tr>
<tr>
<td>Renal cell carcinoma/Wilm’s tumor</td>
<td>&gt; 2 (&gt; 5 for large cancers; no wait for incidental tumor &lt; 5cm)</td>
</tr>
<tr>
<td>Bladder cancer</td>
<td>&gt; 2</td>
</tr>
<tr>
<td>Kaposi sarcoma</td>
<td>&gt; 2</td>
</tr>
<tr>
<td>Leukemia</td>
<td>&gt; 2 (limited data to make recommendations)</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>&gt; 2</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>&gt; 2 (possibly &gt; 5)</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>&gt; 2 (possibly less for localized)</td>
</tr>
<tr>
<td>Testicular cancer</td>
<td>&gt; 2</td>
</tr>
<tr>
<td>Thyroid cancer</td>
<td>&gt; 2</td>
</tr>
<tr>
<td>Skin (nonmelanoma) cancer</td>
<td>0-2 (no wait for basal cell)</td>
</tr>
<tr>
<td>Liver cancer</td>
<td>Unable to give recommendation</td>
</tr>
<tr>
<td>Myeloma</td>
<td>Unable to give recommendation</td>
</tr>
</tbody>
</table>
Bibliography


5. CMS MINUTES. Minutes of the transplant meeting held at CMS. 2010.


