



Trillium
Gift of Life
Network

Clinical Handbook for Heart Transplantation

January 2018

Version 1.0

Disclaimer: The content in this Handbook has been developed through collaborative efforts between Trillium Gift of Life Network and experts from Ontario's heart transplant programs. It is based on available literature and expert opinions at the time of development. The Handbook is not intended to be an exhaustive analysis of all heart transplant literature and practices, and may not reflect all available research and consensus from all experts. Other relevant scientific findings may have been published since completion of the Handbook and it may be superseded by an updated publication on the same topic. While every reasonable effort has been made to ensure the accuracy and validity of the information provided, TGLN and the expert contributors assume no responsibility for any errors or omissions in the content.

Acknowledgements

The Clinical Handbook for Heart Transplantation was developed in conjunction with the expertise of the Provincial Heart and Lung Working Group and members of the transplant community. We would like to acknowledge the following individuals for their contributions in developing this document (listed in alphabetical order):

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We would also like to acknowledge cardiologists and cardiac surgeons from the following transplant centres for their review and feedback during the consultation process: University Health Network, The University of Ottawa Heart Institute, London Health Sciences Centre, and The Hospital for Sick Children.

List of Abbreviations

CAD	Coronary Artery Disease
CVD	Cardiovascular disease
DAD	Discharge Abstract Database
ECFAA	Excellent Care for All Act
ED	Emergency department
HCRS	Home Care Reporting System
IHD	Ischemic Heart Disease
LHIN	Local Health Integration Network
LOS	Length of stay
MOHLTC	Ministry of Health and Long Term Care
NACRS	National Ambulatory Care Reporting System
OAGO	Office of the Auditor General of Ontario
TGLN	Trillium Gift of Life Network
TOTAL	Trillium Organ and Tissue Allocation System

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I. Purpose

The Clinical Handbook for Heart Transplantation includes a clinical pathway and service bundles for heart transplantation which have been developed in response to the *2010 Auditor General's Report on Organ and Tissue Transplantation*, the *2009 Organ and Tissue Wait Times Expert Panel Report*, and as part of the Ministry of Health and Long-Term Care's commitment to quality healthcare and better outcomes.

It aims to identify opportunities to enhance integration of services across the patient care continuum; facilitate efforts to improve existing processes within Ontario's heart transplant centres by reducing unnecessary practice variations and optimizing resource utilization; and inform policy frameworks and implementation approaches to the care of heart transplant patients in Ontario.

The Clinical Handbook includes the following tools to guide the development of policies, procedures, and processes:

1. A clinical pathway for typical heart transplant patients from the time of referral to post-transplantation. The clinical pathway outlines the general process that Ontario patients follow when moving through the transplant system.
2. Services that correspond to each stage of the patient pathway.

To foster partnership and strengthen clinician engagement, the clinical pathway and service bundles were developed using opinions from clinical experts from all Ontario transplant centres, guided by national and international evidence-based guidelines. As a result, the Clinical Handbook is a compendium of evidence based rationale and clinical consensus on guidelines for heart transplant patients.

This document has been prepared as a tool for hospitals and individual providers to support the development of clinical patient pathways for their organizations. The Handbook is not intended to replace the professional skill and judgement of healthcare providers, nor inhibit the development of new and innovative transplant solutions.

II. Improving Quality of Care

At the forefront of Canada's health-care system is a commitment to provide the highest standard of hospital and physician services. In Ontario, the Excellent Care for All Act (ECFAA) supports this by creating greater public accountability, increasing the focus on quality, bringing patient satisfaction to the forefront and basing patient care decisions on the best scientific evidence available. These dimensions of quality are supported by the following six domains:

-) Improve **effectiveness** and reduce variation in clinical outcomes.
-) Improve **appropriateness** by reducing practice variations.
-) Improve **timeliness** across the continuum of care.
-) Improve **efficiency** by reducing unwarranted variation in resource utilization.
-) Improve or maintain **equity** to appropriate health services.
-) Improve **patient centeredness** of health services.

Specific recommendations for the transplantation system were outlined in the *2010 Auditor General's Report on Organ and Tissue Transplantation* and the *2009 Organ and Tissue Wait Times Expert Panel Report*, both of which highlighted the need for a more efficient and equitable allocation system, improved referral practices and more effective oversight for organ transplantation. Since then, new liver and kidney allocation systems have been implemented, standardized practices for referral introduced, and performance indicators and evaluation metrics developed. Such initiatives are aimed at improving both access to transplantation services by reducing geographical differences in wait times and establishing tools for patients and practitioners to ease the transplant process.

Further improvements to quality can be achieved by maximizing system efficiency. Data shows that short and long-term graft survival rates are favourable, but continued improvement remains the goal of all transplant centres. Patient quality of life can also be enhanced by reducing re-hospitalization which according to one study is as high as 64% during the first year after heart transplant (1). Given the significant economic costs of heart transplantation and subsequent re-hospitalization, and desire to further improve outcomes and quality of life, it is imperative that every effort is taken to maximise quality throughout the patient care continuum.

In its report, the Expert Panel specifically raised concern that Ontario does not have standard best practice guidelines for the pre- and post-care of transplant patients, stating that such guidelines are important since they would identify the care that transplant centres and the local community should provide. The Panel recommended:

-) Ontario's transplantation community compile and/or develop pre- and post-care best practice standards and guidelines by organ, and ensure that healthcare providers use these standards and guidelines to inform their care.
-) Trillium Gift of Life Network and the transplantation community establish a system to monitor the use of best practice standards and guidelines for adult and paediatric organ transplantation, and the outcomes of these procedures (2).

These recommendations align with the Excellent Care for All Act (ECFAA) with its increased emphasis on continuous quality improvement supported by evidence informed best practices and standards of care.

The clinical pathway and corresponding services set out in this handbook and the steps taken to monitor their implementation and outcomes are intended to improve the appropriateness and efficiency of transplant care by reducing unnecessary practice variations and optimizing resource utilization, as well as enhancing integration across the patient care continuum.

Clinical Pathways and Practice Guidelines

Clinical pathways are tools used to manage quality in healthcare by standardizing processes. The objectives are to reduce unnecessary variations in practice, improve interdisciplinary cooperation, integrate care, and ultimately, improve clinical outcomes. They are especially useful in complex care systems, such as heart transplant, where care may be delivered by multiple providers at multiple sites over an extended period. Heart transplant referrals require a minimum set of tests and consultations to be completed, as per the *Provincial Transplant Referral Form*. Patients may receive testing as outpatients at referring centres or in hospital as inpatients depending on the severity of their condition. Transplant centres review referrals and may liaise with referring centres to complete additional tests as necessary before scheduling patients for a transplant assessment. During the transplant assessment process, patients are provided with transplant specific education and transplant specialists determine whether patients are eligible to be wait listed. While on the wait list, patients receive ongoing assessments by the transplant centre, which require blood testing and laboratory work, often from community healthcare providers. Once a patient is matched with a potential donor heart, if not already an inpatient, they are admitted and cared for by the transplant centre before, during, and immediately following their transplant surgery. Once transplanted, recipients receive ongoing care from a variety of providers including transplant specialists, cardiologists, family physicians, and other medical practitioners based on their needs. The involvement of multiple providers creates considerable opportunity for variations in practice and resource utilization as the patient moves through the pathway.

The success of practice guidelines and clinical pathways has been documented in a variety of areas. For example, in the treatment of community-acquired pneumonia across nineteen teaching and community hospitals in Canada, implementation of a clinical pathway reduced the use of institutional resources without causing adverse effects on the well-being of patients (3). Other individual clinical pathways, for stroke management, inguinal hernia repair, laparoscopic surgery, pancreaticoduodenectomy, and the management of fractured femoral neck, have been shown to reduce length of stay and total costs of acute hospital admission while maintaining quality of care, improving patient outcomes, interdisciplinary cooperation and staff satisfaction (4).

A systematic review of published literature and analysis of twenty-seven studies involving 11,398 participants found that patients managed according to clinical pathways encountered a reduction in in-hospital complications as compared to usual care. Furthermore, the review presented evidence of decreased lengths of stay and reductions in hospital costs when clinical pathways were implemented (4). More generally, reviews of best practice clinical guideline dissemination and implementation strategies have shown that in the majority of cases, improvements in care are observed (5). In one study of 59 clinical guidelines, the authors concluded that “guidelines improve clinical practice and achieve health

gains when introduced in the context of rigorous evaluations”(6). Specific to heart failure, a recent study estimated that optimal implementation of guideline recommendations could prevent 67,996 deaths a year in the USA alone (7).

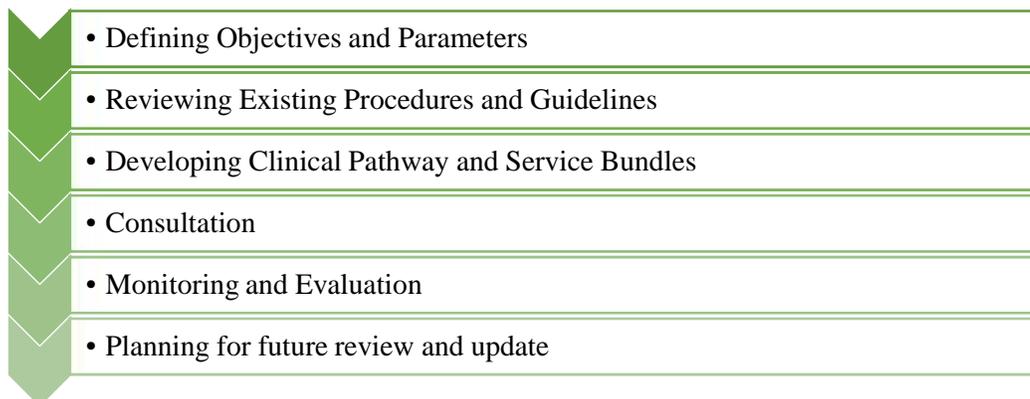
Ultimately, clinical guidelines can improve the experience of patients as they navigate through the transplant process by facilitating integrated care plans along the continuum. With the goal of optimizing care at all stages of the patient continuum, it is intended that this Clinical Handbook will facilitate efforts to improve existing processes in the care of heart transplant patients in Ontario.

III. Methods

In developing the Clinical Handbook, Trillium Gift of Life Network and the Provincial Heart and Lung Working Group took a quality-driven approach for translating evidence into action. The overarching aim was to produce a *quality-driven, evidence-based* clinical pathway and service bundles using an *efficient* and *transparent* methodology for *action-ready* recommendations with *multi-disciplinary applicability*:(8)

-) **Quality-driven** means placing quality improvement at the forefront of clinical pathway and service bundles development, using current best evidence and multidisciplinary consensus to prioritize recommendations. Selection of key action statements is driven by opportunities to promote best practices, reduce unnecessary variations in care, and minimize inappropriate care or resource utilization.
-) **Evidence-based** means supporting all decisions with the best available research evidence identified through systematic literature review and expert consensus (i.e. ISHLT, CCS, and physician & surgeons from all centres).
-) **Efficient** clinical pathway and service bundles make maximum use of available resources to create a timely product, moving from conception to publication within a reasonable timeframe.
-) **Transparent methodology** is explicit, reproducible, and applied consistently so guideline users can link recommendations to the corresponding level of evidence, benefit-harm-cost relationship, and the roles of values and patient preferences in decision making.
-) **Action-ready** recommendations tell providers what to do, to whom, under what specific circumstance, using unambiguous language that facilitates implementation and measurement.
-) **Multi-disciplinary** validity and applicability means that all stakeholders (e.g., primary care, specialists, allied health, nursing, consumers) are part of the development and implementation processes.

To achieve these goals the following systematic process was used:



The following sections describe each of these steps in further detail.

Defining Objectives and Parameters

Objectives

In defining the objectives for developing a clinical pathway and service bundles, the Working Group was guided by the following key question:

How can Ontario's transplant system provide the best quality of care to achieve the best possible outcomes for heart transplant patients?

The Working Group agreed that the Clinical Handbook was an opportunity to develop and implement best practice guidelines throughout the transplant patient continuum, and determined that it must answer the following questions:

-) **Who** should be defined as the patient population(s)?
-) **What** practices and services should be employed in the treatment of transplant patients?
-) **Where** can transplant patients expect to receive their treatment?
-) **When** in their continuum of care can transplant patients expect to receive certain aspects of their care?

These guiding questions ensured that the patients' best interests remained at the centre of the development of the clinical pathway and service bundles.

Parameters

From the outset, the Working Group identified the clinical population as being all patients in Ontario who are potentially eligible to receive a heart transplant. Because of differences in service needs, separate clinical bundles were created for adult and paediatric patients. This decision followed consultation with paediatric specialists and is due in part to anatomical, physiological, and psychological differences between children and adults, and because the common causes of congestive heart failure in children are often different than those in adults.

To ensure a seamless transition between different stages of the transplant process, the Clinical Handbook encompasses a patient's full continuum of care, beginning at the time of referral to a transplant program and continuing through transplantation and long-term, post-transplant management. In most cases, once a patient is referred and placed on the provincial wait list, the patient remains in the transplant care continuum until end of life.

These parameters guided the development of the Clinical Handbook to ensure that full and proper consideration was given to all patient populations throughout their transplant continuum of care.

Reviewing Existing Procedures and Guidelines

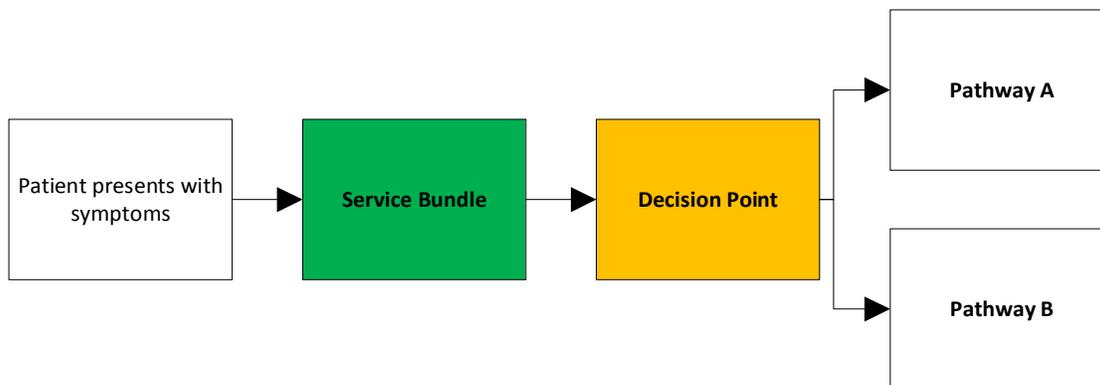
The Clinical Handbook contains a set of recommended practices reviewed and agreed upon by the Working Group and through wider consultation with the transplant community. In keeping with the ECFAA commitment to evidence-based care, considerable attention has been paid to ensure that the practices recommended here are supported by the best available evidence. A review was carried out of existing practices at each of Ontario's heart transplant programs, as well as published national and international clinical guidelines currently utilized in the management of heart transplant patients throughout the world. This involved a detailed review of the following:

-) Standard Operating Procedures from each of Ontario's heart transplant programs
-) Clinical guidelines from the following organizations:
 - o ISHLT Guidelines for the care of heart transplant recipients (2010)
 - o CCS Consensus Conference Update of Cardiac Transplantation (2008)
 - o Listing Criteria for Heart Transplantation: ISHLT Guidelines for the Care of Cardiac Transplant Candidates (2006)
 - o The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: A 10 year update (2016)
 - o CCS Consensus Conference on Cardiac Transplantation (2001)
 - o BC Transplant

The analysis was used to determine what services and procedures were carried out during a patient's care continuum at each of Ontario's heart transplant centres. A full list of services was then compiled and compared with the clinical guidelines to determine if they could be considered best practice.

Developing Clinical Pathway and Service Bundles

The clinical pathway model is structured around the parameters defined for the episode of care. The model describes the pathway of each patient case, from their initial presentation with symptoms warranting consideration of a transplant, through the subsequent components of care that they receive, before reaching an endpoint in their care. An exception to an endpoint of care would be in the post-transplant care phase, which would continue in partnership with the community until the time of the patient's death. The pathway presents the critical decision points and phases of treatment within the continuum of care. Decision points provide patient-specific criteria for whether a particular case proceeds down one branch of the pathway or another. Once patients move down a particular branch, they then receive a set of recommended practices that are clustered together as a bundle. Service bundles represent the major phases of care that patients receive during the transplant process. Figure 1 provides an illustrative example of a service bundle and assessment point:



Through the development of the clinical pathway, the Working Group identified five service bundles corresponding to the key stages in the patient care continuum:

1. **Pre-Transplant before Listing: Referral and Transplant Assessment** - the period before placement on the transplant wait list. It includes the referral package and services required during transplant eligibility assessment.
2. **Pre-Transplant after Listing: Wait List Period** - the period after placement on the wait list, but before the transplant operation.
3. **Preoperative Assessment and Transplant Surgery** - the period from when an organ is matched to the patient, including the preoperative assessment and the surgical procedure.
4. **Post-Transplant: During Hospital Admission** - the period following the transplant operation while the patient is in hospital before discharge.
5. **Post-Transplant: After Discharge** - the period following hospital discharge.

Services for each stage were then categorized into the following two groups:

) **Bundled services:**

These are services that are an essential part of the patient pathway and have a standard expected duration and frequency. For these services, a minimum standard frequency for the typical transplant patient at each phase of the care continuum was assigned. For example, ECG is a bundled service that should take place one time before listing and annually after listing during the wait list period. It is important to note that the set frequencies do not limit every patient's specific service needs. Although the bundles may state that patients should have an ECG annually while on the wait list, some patients may require this more often.

) **Unbundled Services:**

These are services that can potentially be provided to transplant patients but cannot be predicted and/or assigned a standard frequency for a given patient population. Included in this group are services whose frequency varies considerably across centres or services that are required for a patient based on the physician's overall assessment of their health and needs. These services should be provided at the physician's discretion. For example, patients with abnormal renal function should prompt further investigation, including renal ultrasound, estimation for proteinuria, and evaluation for renal arterial disease.(9) Therefore, this service is

recognized and included within the list of potential services, but is not assigned a standard frequency and duration.

Using the expertise of Ontario clinicians, published guidelines, and available data, TGLN provided each transplant program with a draft of the developed service bundles. TGLN solicited feedback from each of the heart transplant centers in Ontario and ensured they had an opportunity to respond to the content in the Clinical Handbook. The centres were asked the following key questions:

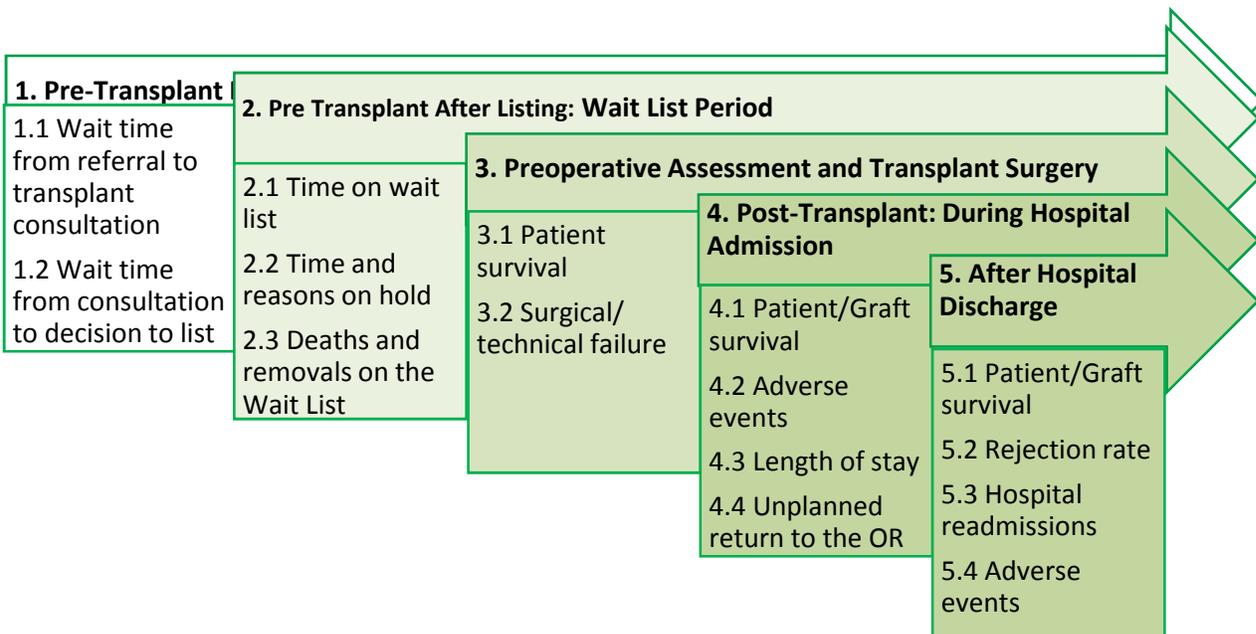
-) Are there any services identified that should not be included in the service bundles?
-) Are there any services that were not identified in the service bundles but should be included?
-) How are the services outlined in the service bundles similar or dissimilar to current practice at your centre?
-) What resources would be required to implement these practices?
-) Are there any barriers to implementing these practices at your centres? Are there any enablers to implementing these practices at your centres?

To ensure transparency in the consultation process, all feedback was collated, with a summary provided to each of the transplant centres detailing the action taken on proposed changes to the service bundles. Centres were then given an opportunity for final review of the revised bundles and asked to submit any final comments.

Monitoring and Evaluation

Efforts to regularly monitor and evaluate the heart transplantation system in Ontario are taken to improve the transplant process and identify opportunities for further improvement. With the expertise of the Provincial Working Groups, TGLN has identified key performance indicators for each stage of the patient care continuum that will help clinicians and administrators monitor quality of care and identify associated opportunities for improvement within their centres.

The following diagram provides a sample of the key process and outcome for each phase of the care continuum.



Indicators during the pre-transplant phases of the care continuum focus on timely transplant assessment, consultation, and wait list management to promote patient safety and timely access to transplant. For the surgical and post-transplant phases, the focus is on patient outcomes, such as patient death, graft failure, length of stay and hospital readmissions and adverse events. Although these are baseline quality indicators that will be collected for all transplant patients, TGLN has worked with the Heart and Lung Working Group to develop definitions that would be most relevant for heart and lung transplant patients.

As part of the TGLN's quality improvement framework, performance indicators will be reported and distributed to transplant programs. Transplant programs may use the reports to evaluate their own processes at each stage of the care continuum and enable centres to track, audit, and evaluate the implementation of the clinical pathway and best practice services within their centres. Through such monitoring, variances can be identified, progress monitored, and practices refined over time to improve patient outcomes.

TGLN, in collaboration with the Heart and Lung Working Group will utilize the performance indicators to monitor and evaluate the transplant system as a whole. The Group may review the current state of the system and make recommendations to support practice changes where notable variations have been identified. Indicators will be reviewed regularly to ensure they remain relevant and align with quality objectives to promote ongoing improvement at both hospital and system levels.

Plan for Future Review and Update

The clinical pathway and service bundles will be revised when appropriate to ensure developments in heart transplant best practice are reflected. Upon the release of new or updated best practise guidelines, new evidence, or policy changes TGLN will conduct a review of the Clinical Handbook. If no guidelines are published, the Clinical Handbook will be reviewed every 2 years by the Provincial Heart and Lung Working Group. Comments received will be incorporated and reviewed by the Working Group as necessary.

IV. Overview of Heart Transplantation

Congestive heart failure (CHF) is one of the major health problems in Canada. There are 600,000 people living with heart failure, with an estimated 50,000 new cases being diagnosed every year (10). Despite major advances in medical therapy for CHF, cardiac transplantation is still the most effective treatment for patients with end-stage heart failure (11).

A heart transplant is the surgical replacement of a person’s severely diseased or damaged heart with a healthy heart from a human donor. It is performed when congestive heart failure or heart injury cannot be treated by any other medical or surgical means. Patients who may need a transplant usually have one of two problems; irreversible damage to the heart because of coronary artery disease that has resulted in severe heart attacks or myocardial infarctions, or cardiomyopathy, in which the heart is unable to contract normally because of damage to the muscle cells. Occasionally, other forms of heart disease require transplantation, such as congenital heart defects, which are structural problems present at birth.

Heart transplantation is generally reserved for patients who are estimated to have poor prognosis, an elevated risk of dying from heart failure in the following year (~15-20%) without the transplant, and who cannot be helped by conventional medical therapy. It not only improves the quality of life for patients, but has shown to be a life-prolonging procedure. In Canada, it is the third most common organ transplant operation, after kidney and liver transplants.

Overall, heart transplant success rates in Canada are favourable, with survival after transplant having improved over the past decade. As shown in table 1, one-year survival rates are around 90%, and five-year survival rates are over 80%. Improved outcomes can be attributed to progress in perioperative management, patient selection, management of rejection, and management of candidates with ventricular assist devices (VADs). In particular, advances in implantable devices have revolutionized the way end-stage heart failure patients are managed as this strategy has proven to be an effective treatment option while patients await transplant, as indicated by better functional status, quality of life and reduced adverse events (12).

	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
3 Months	88.6	86.8	89.7	95.0	90.8	88.6	92.1	91.3	95.0	95.2
1 Year	85.6	86.2	88.4	92.4	89.0	86.7	90.7	89.4	90.6	
3 Years	82.5	83.2	86.5	89.3	87.1	82.2	87.8			
5 Years	80.7	82.6	85.2	88.0	85.3					

Source: Canadian Organ Replacement Register, 2015, Canadian Institute for Health Information

For heart transplant patients, cardiovascular/cerebrovascular diseases, cancer, and cumulative exposure to immunosuppression are some of the key concerns in the transplant community (13).

V. Heart Transplantation in Ontario

Data and Volumes

Over the past decade around 700 heart transplantations have been performed in Ontario. There are four centres at which heart transplant procedures are performed. There are three adult heart transplant programs: University Health Network, the Ottawa Heart Institute and London Health Sciences Centre. The paediatric heart transplant program is located at the Hospital for Sick Children.

Table 2 shows both the number of heart transplants that have been completed in Ontario since 2010 as well as the number of patients on the wait list at the end of each calendar year.

	2010	2011	2012	2013	2014	2015
Transplants	68	61	74	83	69	72
Wait List Snapshot at End of Year	58	68	60	61	63	76

Source: TGLN, 2016

Table 3 shows the average number of days from being wait listed to heart transplantation from 2010 to 2015. Since 2010, wait times have followed a downward trend, with the most recently transplanted patients waiting an average of around six months from listing date to transplant. Current and future initiatives will be aimed at further reducing wait times.

2010	2011	2012	2013	2014	2015
214.6	212.0	219.1	180.0	173.7	186.7

Source: TGLN, 2016

Trillium Gift of Life Network

Trillium Gift of Life Network (TGLN) is an agency of the Ontario Ministry of Health and Long-Term Care established in 2002 with responsibility for co-ordinating the donation of organs and tissue in Ontario. Its mandate was extended to include transplantation in 2011/12 following recommendations from the *2010 Auditor General's Report on Organ and Tissue Transplantation* and the *2009 Organ and Tissue Wait Times Expert Panel Report* for an integrated donor and transplant system.

TGLN's transplant strategy aims to support the development of a sustainable end to end transplant system and to continually strive to improve the dimensions of quality, safety, effectiveness, access, patient centered care – all to enable better patient outcomes. This includes developing a provincial transplant system that provides equitable access through standardized processes and planning to enable better patient outcomes, and harmonizing the patient journey across the transplant continuum from pre-transplant through to post-transplant care.

Strategies to further enhance the provincial heart transplant system are facilitated by TGLN through the Provincial Heart Lung Working Group, which includes medical and administrative membership from each of Ontario's heart transplant programs. The Working Group's mandate is to consider all aspects related to the transplant patient's journey and recommend evidence-based policies and practices to ensure equitable access to quality patient care.

TGLN and the Provincial Heart Lung Working Group has implemented the following key initiatives aimed at improving patient access and equity, and the quality of care along the patient continuum:

) **Provincial Heart Allocation Algorithm**

As there are not enough donor hearts to meet the demand, every effort is made to ensure that allocation is as fair and equitable as possible. The Working Group regularly reviews and updates the heart allocation algorithm to ensure that it gives fair consideration of candidates' circumstances and medical needs, as well medical utility, by trying to increase the length of time patients and organs survive.

) **Referral and Listing Criteria**

In its report, the Auditor General recommended that TGLN, in conjunction with transplant hospitals and physicians, should "determine the best way to communicate referral criteria to non-transplant physicians, so that individuals who would benefit from a transplant (including from a quality-of-life perspective) are added to the wait list."

TGLN has since taken measures to improve the referral process so that all patients who meet the criteria can be referred for transplant specialist consultation and assessment. These include:

- Standardized referral form for external referrals to ensure appropriate information is sent to transplant centres;
- Standardized referral and listing criteria to increase transparency and help support equitable access to transplant.

) **Ontario Clinical Guidelines for VADs**

The Heart Lung Working Group has introduced clinical guidelines for Ventricular Assist Device (VAD) practices along the patient continuum. It includes a set of evidence-based and clinical consensus recommendations that can be used to advance best practices and quality of care for VAD patients. The guideline applies to bridge-to-transplant implants and offers recommendations on indications, patient evaluation, patient management, and follow up care.

Following the Ontario Health Technology Advisory Committee (OHTAC) review of VADs for destination therapy, published in February 2016, TGLN is working in partnership with CCN to develop an addendum to the Clinical Guidelines addressing OHTAC's recommendations and providing specific guidelines on VADs for destination therapy.

) **Performance Measurement and Monitoring**

In May 2013, TGLN finalized a set of performance indicators to be developed as part of its quality framework for system monitoring and improvement. This includes thirteen key metrics from the Auditor General recommendations such as patient wait time, organ yield, deaths and

removal on the wait list, patient and graft survival, and organ disposition. TGLN is also responsible for monitoring VAD volumes, for all indications such as bridge to transplant as well as destination therapy.

The development of the Clinical Handbook is part of the ongoing provincial initiative to facilitate Ontario's goals of consistently delivering high quality heart transplant care across the province.

Transplantation Process

Pre-Transplant Before Listing: Referral and Initial Assessment

This phase refers to the period before placement on the heart transplant wait list. It includes the referral package and services required during transplant eligibility assessment.

Heart transplantation should be considered for patients with advanced heart failure that is either not amenable to further or progresses despite medical and surgical therapy. Guidelines for medical practitioners to utilize when referring a patient to a transplant program for assessment are outlined in the *Provincial Heart Transplantation Referral and Listing Criteria* (Appendix B). The criteria identify the requirements which have to be met for evaluation to be considered, and lists conditions that constitute absolute contraindications to heart transplantation.

The Heart Transplant Referral Form (Appendix C) includes the patient information, medical history, and lab and diagnostic testing results required for the referral package. Once a referral is received, the referral package is reviewed to determine whether candidates are eligible for a transplant assessment. Candidates will undergo further testing and consultation to evaluate their eligibility for transplant. The evaluation is aimed at assessing the degree of advanced heart failure and management to date, options for bridging to transplantation, the chances of recovery from surgery, maximizing short- and long-term survival, and assessing the potential impact of transplantation on quality of life. Evaluation of the suitability of heart transplant candidates includes medical, surgical, immunologic, and psychosocial assessments.

For candidacy, patients will have to fulfill various criteria. Though the relation between functional capacity and survival in heart failure is well established, the decision on candidacy for heart transplant should take into account all clinical data following multidisciplinary discussion rather than focussing on peak oxygen uptake alone (14,15). Blood is drawn for serological and infectious disease testing as patients should be free of active infection, whether of viral, bacterial or fungal origin. Testing of HBV and HCV serology is particularly important, due to their association with decreased post-transplant outcome (16). Other infectious screening criteria, including for HIV, CMV, and EBV are outlined by the ISHLT in its listing criteria for heart transplantation (9).

Patient evaluation should also investigate other risk factors and contraindications. Impaired renal function is an independent predictor of mortality following heart transplantation and should be assessed by estimation of GFR (9,17). Ultrasound should be used to distinguish intrinsic renal damage from reversible dysfunction secondary to congestion and low cardiac output (18). Liver dysfunction is also a predictor of adverse outcome following transplant and should be assessed using standard liver function tests and advanced consultation and testing on an individual basis.

Screening for other common risks to transplantation should also be completed during the transplant assessment. For example, active malignancy is an absolute contraindication to heart transplant and using the Ontario Cancer Screening guidelines, patients should be screened for cancer at the time of evaluation (19).

Given the importance of adherence to therapy in transplant outcomes, all patients should have a pre-transplant psychosocial evaluation to assess for cognitive impairment, mental illness, risk of non-adherence to therapy and drug or alcohol abuse, and social and emotional supports (16). Patients should also receive transplant education so that they can make an informed decision about whether or not to proceed with transplant. Education should include the risks of the operation, side effects, implications of long-term monitoring including biopsies, immunosuppression, post-transplant morbidities, follow-up, short and long-term outcomes, and mortality estimates.

A full list of consultations, diagnostics and lab tests for patients undergoing assessment is outlined in the service bundle called ***Pre-transplant Before Listing: Referral and Initial Assessment***. The referral and transplant assessment process is carried out at both referring centres and transplant centres either as an outpatient or inpatient, and may take several months to complete. The referral and transplant assessment process

Pre-Transplant After Listing: Wait List Period

This phase refers to the time period after placement on the wait list, but before the transplant operation.

Once the transplant team has agreed to pursue transplantation, patients are placed on the Ontario Heart Transplant Wait List. Donor organs are allocated on principles of equity and fairness, taking into consideration blood type, medical urgency, organ suitability, medical status, and wait time.

As the waiting time for a heart transplant can vary from a few days to several years, patients will continue to be monitored by the transplant program to ensure their ongoing eligibility for transplant. A full list of consultations, diagnostics and lab tests is outlined in the service bundle called ***Pre-transplant After Listing: Wait List Period***. Depending upon the patient's condition, day to day management of the patient and blood testing will be completed by the referring centre for outpatients and in hospital for inpatients, which are sent and reviewed by members of the multidisciplinary transplant team.

If a patient develops a new medical issue or is temporarily unable to receive a transplant while on the wait list, they will be placed on hold. For example, if a patient develops an infection that is a contraindication to transplant, they will be placed on hold until it has been resolved. Candidates with an on hold status are not eligible for organ allocation, but will continue to accrue wait time.

Preoperative Assessment and Transplant Surgery

This phase refers to the time period from when the patient is alerted that an organ match has been found and accepted by the Transplant program, to the pre-operative assessment and the surgical procedure.

TGLN notifies the candidate's transplant program of potential deceased organ donor matches, and the transplant program contacts the patient once an organ has been accepted for a specific patient based on the criteria outlined above. Patients not in hospital will be asked about the current state of their health and

if no new medical problems have developed, they will be admitted to the hospital for transplant. All patients will receive a final assessment for surgical suitability before undergoing transplant surgery. The final assessment for transplant surgery can include surgical, cardiology and anesthesia consultations as well as lab and diagnostic testing. Each program has expertise in transplantation, advanced heart failure management and the flexibility to consult with other medical specialties and multidisciplinary teams to inform complex care practices beyond the scope of existing recommendations.

A full list of consultations, diagnostics and lab tests is outlined in the service bundle called ***Preoperative Assessment and Transplant Surgery***. A multidisciplinary clinical team completes the patient assessment, prepares the patient for transplant, and performs the transplant surgery. The timing of a heart transplant surgery varies depending on the complexity of the procedure.

Post-Transplant: During Hospital Admission

This phase refers to the time period following the transplant surgery until the day of hospital discharge.

Transplant programs are responsible for patient management during the post-transplant, hospital admission phase. During this phase, clinical teams closely monitor patients to ensure the necessary testing and interventions are completed. They are closely monitored in the ICU where they will remain until stabilized before being transferred to the designated ward. A full list is outlined in the service bundle for adult post-transplant: during hospital admission.

Patients begin their immunosuppression therapy which is based on the transplant recipient's immunological risk and donor factors. Agents are used in combination to achieve sufficient immunosuppression, while minimizing the toxicity associated with individual agents. Most patients receive triple-drug immunosuppressive therapy, consisting of calcineurin inhibitors, purine antimetabolites and steroids. Since the risk for acute rejection is highest in the first 3 months after transplantation, higher doses are used during this period, and then reduced thereafter in stable patients to minimize toxicity (20).

Most patients can be transferred to the designated ward within 2-5 days, once hemodynamically stable and no longer requiring critical care management and surveillance. Patients remain in the hospital until they no longer require in-hospital care and/or monitoring.

Post-Transplant: After Discharge

This phase refers to the time period following hospital discharge.

Following discharge from hospital, the transplant team and appropriate healthcare providers monitor patients through outpatient clinic visits, ensuring the necessary testing is completed, interpreting lab and diagnostic results, and collaborating with other members of the multidisciplinary team as required. The transplant team also monitors and adjusts immunosuppression therapy to prevent organ rejection.

The majority of cardiac transplant recipients will have at least one episode of rejection in the first year after transplantation (21). Because symptoms are often asymptomatic, routine testing for rejection is standard practice (22). The endomyocardial biopsy remains the best practice standard in rejection

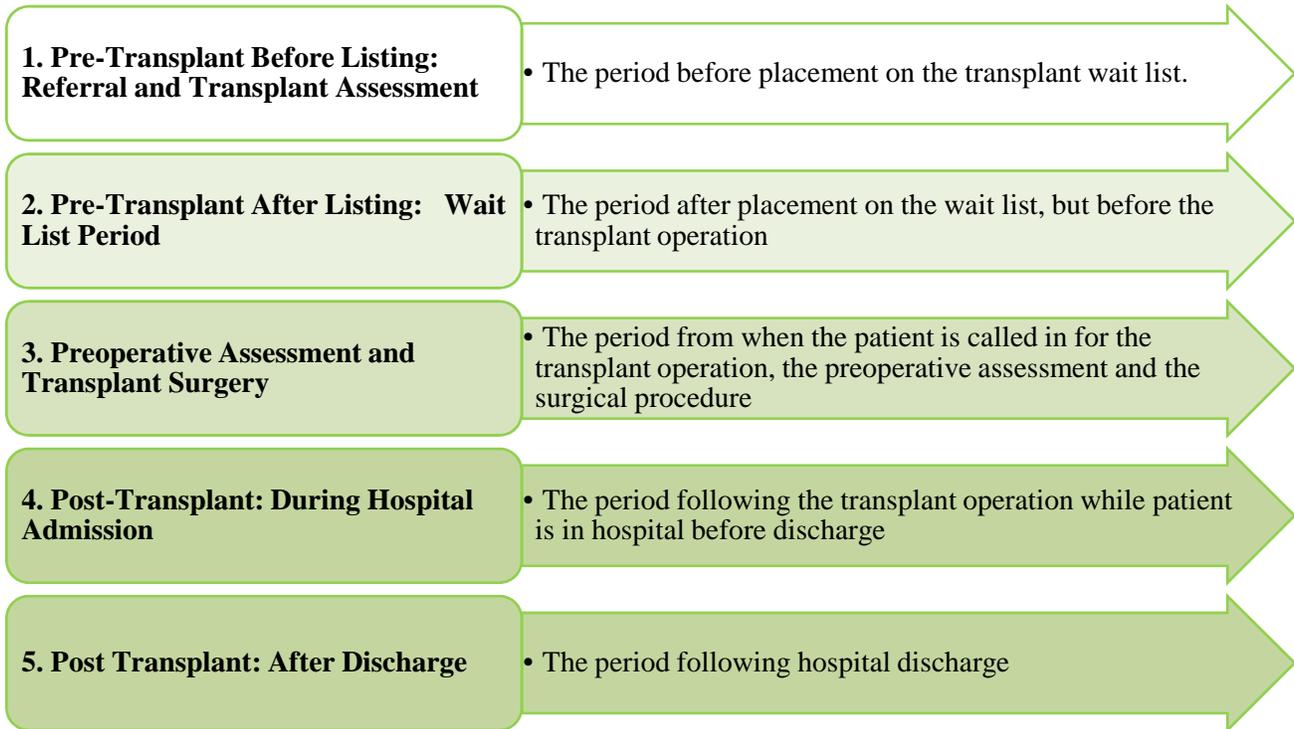
surveillance, the purpose of which is to assess for myocardial damage in the form of acute cellular rejection (ACR) or antibody-mediated rejection (AMR) (23).

Heart transplant recipients should also be screened for infections, which are most likely to occur in the weeks immediately after surgery and after augmentation of immunosuppression for rejection(20). There is higher risk related to viral replication or reactivation (e.g. CMV, EBV) in the first 6 months post-transplant in addition to increased risk of pneumocystis carinii, and toxoplasmosis, hence the need for prophylactic antiviral and/or antimicrobial agents during this time period. As well, donor infections that were not captured during the donor screening process, such as hepatitis or mycobacteria can surface during this period. Beyond six months after transplantation, conventional infections seen in the general population tend to occur. Basic testing should include a complete blood count, hepatic and renal panels and a chest x-ray to detect infections or any signs of rejection (20,24).

Cardiac allograft vasculopathy (CAV) is an accelerated form of coronary artery disease which is also a major causes of mortality after heart transplantation, affecting up to 50% of patients within 5 years of surgery (24). Diagnosis of CAV is predominantly made by coronary angiography, while intravascular ultrasound (IVUS) in conjunction with coronary angiography can be used to exclude donor coronary artery disease, detect rapidly progressive CAV, and provide prognostic information (23). Other key causes of morbidity and mortality post-transplant include malignancy, renal dysfunction, hypertension, hyperlipidemia, amongst others and require routine screening, evaluation and treatment. A full list of tests and diagnostics for this phase of care is outlined in the service bundle for adult post-transplant: after discharge.

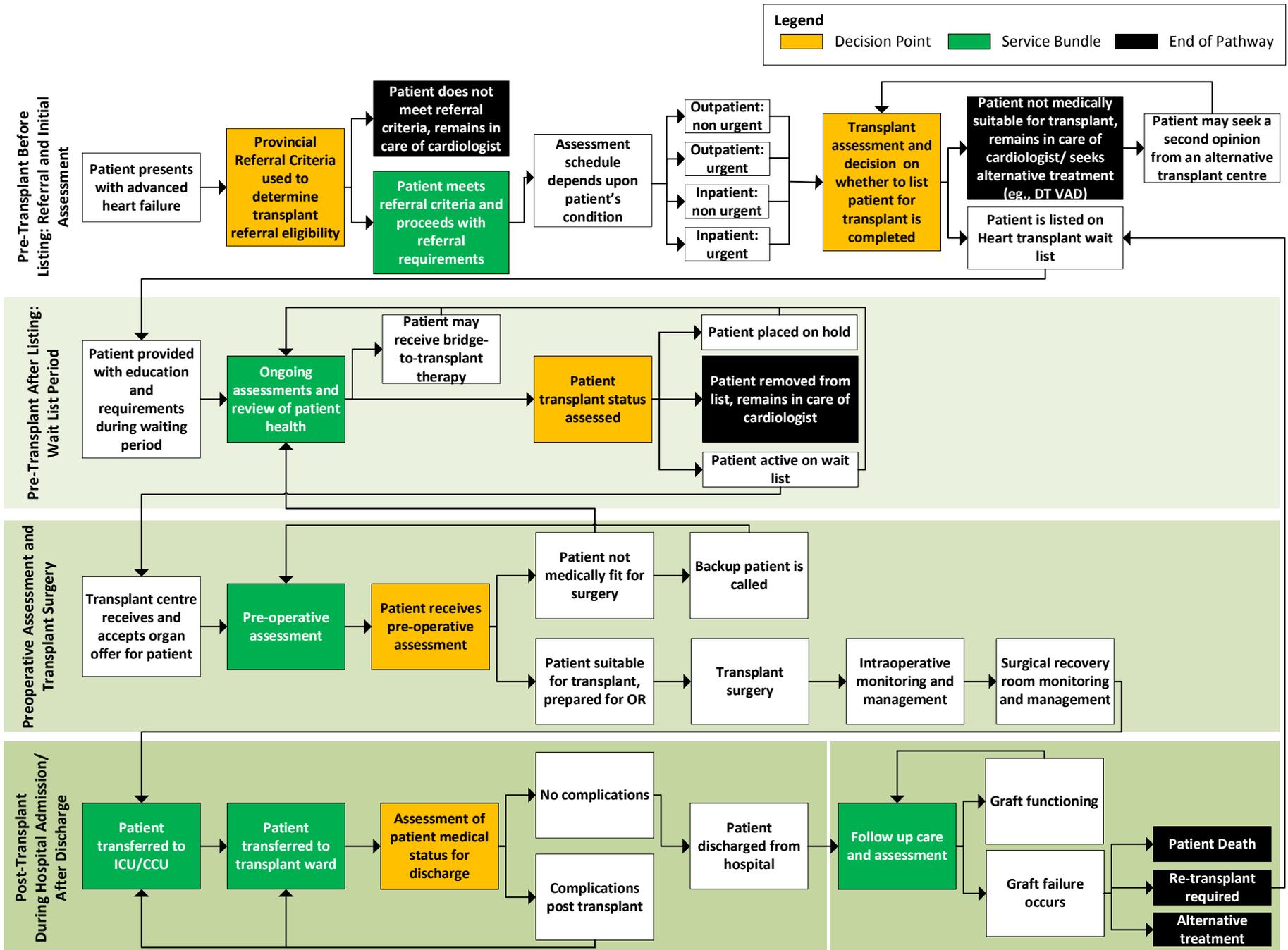
VI. Clinical Pathway for Heart Transplantation

The clinical pathway outlines the process that the typical Ontario patient can expect when moving through the transplant system. It is categorized into the following five key stages of the patient care continuum:



The pathway is intended to be a general guide to the transplant process and identify what patients can expect to receive during the specific time periods. It presents decision points and phases of treatment (service bundles) within an episode of care. Because the decision points determine whether or not a patient moves to the next stage of the transplant process, Appendix B outlines the criteria for patient referral and listing. The list of services for each service bundle are detailed in section VII.

The clinical pathway and service bundles should be used in tandem to guide the care of heart transplant patients in Ontario.



VII. Service Bundles

The Service Bundles outline the full scope of services and the frequencies with which they may be provided to the typical transplant patient at each stage of their transplant care continuum. The timing of when these services should be administered during the care continuum is indicated in the Clinical Pathway. Although all services will be provided as part of the transplant process, not all will be carried out at the transplant centre.

Because of differences in service needs for adult and paediatric patients, separate service bundles have been created for each group.

Unbundled services, which refer to services which cannot be predicted and/or do not have a standard frequency for a given patient population are not listed.

The Services Bundles do not to replace the professional skill and judgment of healthcare providers, but rather ensure minimum standards of care are met for all patients regardless of where care is being provided. They cannot be used to apply to all patients in all circumstances and cannot be used as a legal resource.

Adult Heart Transplant Bundle

Adult Pre-Transplant Before Listing: Referral and Initial Assessment

Clinical Care: The transplant programs are responsible for determining whether the patient is medically suitable to receive a transplant. Once the referral is received, the transplant programs work to complete the required consultations, diagnostics, and lab testing to enable the multidisciplinary clinical team to assess the patient for transplant eligibility.

The assessment schedule is dependent upon the patient’s condition and will be carried out as either an inpatient or outpatient. Patients are registered in the TGLN registry. Patient management during this phase is supported by the following personnel:

-) RN, APN, cardiologist, transplant surgeon and other specialists as needed
-) Allied health care (social work, physiotherapy, occupational therapy, pharmacy, and nutrition)
-) Administrative support

In addition to the recommendations below, all transplant hospitals are expected to have their own protocols on how to treat complications common to all heart failure patients. Each program has expertise in advanced heart failure management and the flexibility to consult with other medical specialties and multidisciplinary teams to inform complex care practices beyond the scope of existing recommendations.

Clinical Visits and Consultations		Lab Testing	
Transplant Education	ongoing	CBC	one time
Social Worker Consultation	one time	Electrolytes	one time
Dietitian Consultation	one time	Total bilirubin, Direct Bilirubin, Albumin, Total Protein, ALP, AST, ALT, GGT, BNP	one time
Physiotherapist Consultation	one time	Calcium, phosphate, LDH, urea, creatinine, magnesium, glucose	one time
Mental health assessment (neuropsychologist, psychiatry, psychology consultation)	one time	Cholesterol, Triglycerides, HDL, LDL (fasting)	one time
Surgical/Anaesthesia Consult	one time	Fasting glucose, random glucose	one time
Diagnostic Imaging		Ferritin, serum iron, TIBC, Urate	one time
		ECG	one time
		Chest X-ray	one time
		Non-invasive stress test/exercise test / CPET (Echo, MUGA)	one time
		Cardiac catheterization (angiogram, LHC, RHC)	at least one time and as needed
Immunologic Evaluation		Thyroid (TsH)	one time
		PT, PTT, INR	one time
HLA antibody screen and antibody specificities		24 hr. urine Creatinine clearance/protein, <i>for diabetic patients only</i>	one time
		GFR	one time
Ultrasound		HgbA1c	one time
		Folate	one time
		Urinalysis	one time
		Stool OB	one time
		ABO blood group determination	one time
Abdominal ultrasound Doppler (femoral, carotid, vascular)		Other Tests/ assessments	
		Minimum of Bedside Spirometry	one time

Services continued on next page

Adult Pre-Transplant Before Listing: Referral and Initial Assessment

Continued from previous page

Infectious Profile	
CMV Antibody (IgM, IgG)	one time
EBV Antibody (IgM, IgG)	one time
Hepatitis A antibody	one time
Hepatitis B core antibody	one time
Hepatitis B surface antibody	one time
Hepatitis C antibody	one time
HIV	one time
HTLVI & II	one time
HSV	one time
Toxoplasmosis	one time
Varicella	one time

Adult Pre-Transplant After Listing: Wait List Period

Clinical Care: Transplant programs are responsible for determining whether the patient remains medically suitable to receive a transplant. Transplant programs will complete the required consultations, diagnostics, and lab testing to enable the multidisciplinary clinical team to assess the patient for ongoing transplant eligibility. While the patient is on the wait list, ongoing assessment is carried out as either inpatient or outpatient. Patients should be considered for the shingles vaccine prior to transplantation. Patient management during this phase is supported by the following personnel:

-) RN and APN, MD
-) Allied health care (social work, physiotherapy, occupational therapy, pharmacy, and nutrition)
-) Administrative support

In addition to the recommendations below, all transplant hospitals are expected to have their own protocols on how to treat complications common to all heart failure patients. Each program has expertise in advanced heart failure management and the flexibility to consult with other medical specialties and multidisciplinary teams to inform complex care practices beyond the scope of existing recommendations.

Clinical Visits and Consultations	
Transplant Education	ongoing
Dental Consultation	annual
ID & Immunology Consultation	one time

Infectious Profile	
CMV Antibody (IgM, IgG)	annual
EBV Antibody (IgM, IgG)	annual
EBV PCR	annual
Toxoplasmosis	annual
Hepatitis B surface antibody	annual
Hepatitis C antibody	annual
HIV	annual
HTLV I & II	annual
TSH	annual

Laboratory Testing	
Routine lab work (blood and urine)	q3 months

Immunologic Evaluation	
HLA antibody screen and antibody specificities	one time then as needed

Imaging	
ECG	annual
Chest X-ray	annual or as needed
None-invasive stress test (Echo, MUGA), CPET	annual
Cardiac catheterization (RHC)	Q3-6 months

Adult Preoperative Assessment and Transplant Surgery

Clinical Care: The transplant programs are responsible for patient management during the preoperative assessment and transplant surgery phase of the transplant process. TGLN liaises with programs regarding potential deceased organ donor matches, and the program contacts patients once a match has been found. Patients will receive a final assessment before they are admitted for surgery. The clinical team completes the patient assessment, prepares the patient for the transplant, orders and administers any preoperative medications, and performs the procedure. Patient management and monitoring for the perioperative period is supported by the following personnel:

-) RN and APN, Cardiologist
-) Surgical team
-) CCU/ICU
-) Administrative support

In addition to the recommendations below, all transplant hospitals are expected to have their own protocols on how to treat complications common to surgery and heart failure patients. Each program has expertise in transplantation, advanced heart failure management and the flexibility to consult with other medical specialties and multidisciplinary teams to inform complex care practices beyond the scope of existing recommendations.

Consultations

Anesthesia	one time
Transplant education & clinical trials	one time
Cardiology	one time

Imaging

Chest X-Ray	one time
ECG	one time

Treatment

Peripheral IV insertion	one time
Swan-Ganz	as required

Laboratory Testing

CBC	one time
Electrolytes	one time
Total bilirubin, Bilirubin, Albumin, Total Protein, ALP, AST, ALT, GGT, Glucose	one time
PT, PTT, INR	one time
Reticulocyte Count	one time
Urinalysis, urine C&S	once time
Type and Screen	one time
Crossmatch	one time

Transplant Surgery

Preoperative assessment and monitoring by surgical team
 Transplant surgery including transplant surgeon, surgical team, anesthesiologist, operating room staff, and all other resources required during the surgery.

Immediate post-transplant monitoring and management

Post-Anesthetic care (recovery phase)
 Post-operative care unit
 Diagnostic and laboratory assessment

Adult Post-Transplant: During Hospital Admission

Clinical Care: Transplant programs are responsible for patient management during the post-transplant, hospital admission phase. During this phase, clinical teams continue to monitor patients, administer pain medication, and ensure necessary testing and interventions are completed. Patients will initially be monitored in the intensive care unit before being transferred to the surgical ward. Patients also begin their immunosuppression therapy. Ongoing patient management, monitoring, education and nursing care is supported by the following personnel.

-) RN and APN, MD
-) Allied health care (social work, physiotherapy, occupational therapy, pharmacy, and nutrition)
-) Administrative support

In addition to the recommendations below, all transplant hospitals are expected to have their own protocols on how to treat complications common to all transplant and heart failure patients. Each program has expertise in transplantation, advanced heart failure management and the flexibility to consult with other medical specialties and multidisciplinary teams to inform complex care practices beyond the scope of existing recommendations.

Consultations	
Patient education	ongoing
Dietitian	one time
Physiotherapy	ongoing
Pharmacy	ongoing
Transplant Coordinator	ongoing

Imaging	
ECG	once, then as needed
Echo	once, then as needed
Chest X-Ray	once, then as needed

Infectious Disease	
CMV PCR	at least once
EBV PCR	at least once

Immunologic Evaluation	
Immunosuppression levels) weekly for 1 month
) once to 2x/week: 1-6 months
HLA antibody screen and antibody specificities) one time, then as needed

Laboratory Testing	
CBC	daily*
Electrolytes	daily*
Total bilirubin, Bilirubin, Albumin, Total Protein, ALP, AST, ALT, GGT, Glucose	daily*
Calcium, phosphate, LDH, urea, creatinine, magnesium, glucose	daily*
PT, PTT, INR	daily*
Urinalysis	once, then as needed
Immunosuppression levels	daily*
Arterial blood gases	daily*

**in the acute peri-operative period, then as needed*

Treatment	
Pace Wires (dressing and removal)	One time

Other tests/Assessments	
Heart Biopsy + right heart catheterization	once, then weekly until discharge

Adult Post-Transplant: After Discharge

Clinical Care: Transplant programs are primarily responsible for patient management during the post-transplant phase after discharge from the hospital. The transplant team and appropriate health care providers monitor patients through outpatient clinic visits, ensure the necessary testing is completed, interpreting laboratory and diagnostic results and collaborating with other members of the multidisciplinary transplant team as required. The transplant program also monitors and adjusts immunosuppression therapy to prevent organ rejection. Ongoing management and monitoring of patient's transplant is completed by the transplant program and is supported by the following personnel.

-) RN and APN, MD
-) Allied health care (social work, physiotherapy, psychology, occupational therapy, pharmacy, and nutrition)
-) Administrative support

Each program has expertise in transplantation, advanced heart failure management and the flexibility to consult with other medical specialties and multidisciplinary teams to inform complex care practices beyond the scope of existing recommendations.

Consultations

Transplant education	ongoing as needed
Physiotherapy/ Rehabilitation	first 3 months, then as needed
Social work	ongoing as needed

Imaging

ECG	once, then as needed
Echo	Minimum once yearly, then as needed
Bone Mineral Density	once, then as needed
Non-invasive stress tests	once, then as needed
Coronary angiography/ intravascular ultrasound	1, 3, 5, and 10 years as needed
Chest X-Ray	monthly for 3 months, then q1 to 2 years

Immunologic Evaluation

Immunosuppression levels	<ul style="list-style-type: none"> • 1-2/weekly for 1 month • 1/week: 1-6 months • monthly: 6-12 months • q6 -12 months and as needed > 1 year
HLA antibody screen and antibody specificities	<ul style="list-style-type: none"> • q3 months for one year; • Then annual or as needed

Infectious Profile

CMV PCR	once, then as needed
EBV PCR	once, then as needed

Laboratory Testing

Electrolytes, urea, magnesium, creatinine, GFR, glucose	<ul style="list-style-type: none"> • weekly for 1 month • weekly-q2 weeks: 3-6 months • q2 weeks-Monthly: 6-12 months • q3-6 months: ≥ 1 year, then as needed
CBC	<ul style="list-style-type: none"> • weekly for 1 month • weekly-q2 weeks: 3 months • monthly: 6-12 months • q3-6 months: ≥ 1 year, then as needed
Liver Function Tests	q3-6 months or as required
Lipid levels	one time at 3 months, then q6-12 months
Hgb A ₁ C for diabetic patients only	q6 months, and as needed

Testing for Increased Risk Donors Heart Recipients

HIV, HCV NAT	At 1 and 3 months
HBV NAT or HBsAg	At 12 months
Anti-HBs, anti-HBc, and either HBV NAT or HBsAg	At 12 months

Other Tests/Assessments

Heart Biopsy	<ul style="list-style-type: none"> • weekly for 4 weeks • q2 weeks: 1-3 months • q3 months: 3-12 months thereafter annually or as needed
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Paediatric Heart Transplant Bundle

Paediatric Pre-Transplant Before Listing: Referral and Initial Assessment

Clinical Care: The transplant programs are responsible for determining whether the patient is medically suitable to receive a transplant. Once the referral is received, the transplant programs work to complete the required consultations, diagnostics, and lab testing to enable the multidisciplinary clinical team to assess the patient for transplant eligibility.

The assessment schedule is dependent upon the patient's condition and will be carried out at either an inpatient or outpatient transplant clinic. Patients who qualify for listing are registered in the TGLN registry. Patient management during this phase is supported by the following personnel:

-) RN, APN, cardiologist, transplant surgeon and other specialists as needed
-) Allied health care (social work, physiotherapy, occupational therapy, pharmacy, and nutrition)
-) Administrative support

In addition to the recommendations below, all transplant hospitals are expected to have their own protocols on how to treat complications common to all heart failure patients. Each program has expertise in advanced heart failure management and the flexibility to consult with other medical specialties and multidisciplinary teams to inform complex care practices beyond the scope of existing recommendations.

Clinical Visits and Consultations	
Transplant Education	ongoing
Social Worker Consultation	one time
Dietitian Consultation	one time
Physiotherapist Consultation	one time
Mental health assessment (neuropsychologist, psychiatry, psychology consultation)	one time
Surgical/Anaesthesia Consult	one time
Child Life Specialist Consultation	one time

Lab Testing	
CBC	one time
Electrolytes	one time
Total bilirubin, Bilirubin, Albumin, Total Protein, ALP, AST, ALT, GGT, BNP	one time
Urea, creatinine	one time
Cholesterol, Triglycerides, HDL, LDL (fasting)	one time
Fasting glucose, random glucose	one time
PT, PTT, INR	one time
Urinalysis	one time
Chromosomes (FISH)	one time
ABO blood group determination	one time

Infectious Profile	
CMV Antibody (IgM, IgG)	one time
EBV Antibody (IgM, IgG)	one time
Hepatitis A antibody	one time
Hepatitis B core antibody	one time
Hepatitis B surface antibody	one time
Hepatitis C antibody	one time
HIV	one time
HSV	one time
Toxoplasmosis	one time
Varicella	one time
Immunoglobulins (IgG, IgM, IgA)	one time
CMV PCR	one time
EBV PCR	one time
Adenovirus	one time
Measles, mumps, rubella (post vaccination)	one time
Adenovirus	one time
Diphtheria (post vaccination)	one time
Pertussis (post vaccination)	one time
Tetanus (post vaccination)	one time
Polio (post vaccination)	one time

Immunologic Evaluation	
Isohemagglutinin titres	one time
HLA antibody screen and antibody specificities	one time

Services continued on next page

Paediatric Pre-Transplant Before Listing: Referral and Initial Assessment

Continued from previous page

Ultrasound	
Abdominal ultrasound	one time
Doppler (femoral, carotid, vascular)	one time

Other tests/assessments	
Head circumference	one time

Diagnostic Testing	
ECG	one time
Chest X-ray	one time
Non-invasive stress test/exercise test (Echo, MUGA)	one time
CT Scan	one time
Cardiac catheterization (angiogram, LHC, RHC)	as needed
Echocardiogram	one time
Cardiac MRI	one time
GFR	one time
Bone Mineral Density	one time

Paediatric Pre-Transplant After Listing: Wait List Period

Clinical Care: Transplant programs are responsible for determining whether the patient remains medically suitable to receive a transplant. Transplant programs will complete the required consultations, diagnostics, and lab testing to enable the multidisciplinary clinical team to assess the patient for ongoing transplant eligibility. While patient is on the wait list, ongoing assessment is carried out as either inpatient or outpatient. Patient management during this phase is supported by the following personnel:

-) RN and APN, MD
-) Allied health care (social work, physiotherapy, occupational therapy, pharmacy, and nutrition)
-) Administrative support

In addition to the recommendations below, all transplant hospitals are expected to have their own protocols on how to treat complications common to all heart failure patients. Each program has expertise in advanced heart failure management and the flexibility to consult with other medical specialties and multidisciplinary teams to inform complex care practices beyond the scope of existing recommendations.

Clinical Visits and Consultations	
Transplant Education	ongoing
Dental Consultation	annual

Laboratory Testing	
Routine lab work (blood and urine)	q3 months

Infectious Profile	
CMV Antibody (IgM, IgG)	q3 months if negative
CMV PCR	q3 months if negative
EBV Antibody (IgM, IgG)	q3 months if negative
EBV PCR	q3 months if negative
Toxoplasmosis	annual
Hepatitis B surface antibody	annual

Immunologic Evaluation	
HLA antibody screen and antibody specificities	q3 months
Isohemagglutinins (if ABO incompatible)	monthly

Paediatric Preoperative Assessment and Transplant Surgery

Clinical Care: The transplant programs are responsible for patient management during the preoperative assessment and transplant surgery phase of the transplant process. TGLN liaises with programs regarding potential deceased organ donor matches, and contact patients once a match has been found. Patients will receive a final assessment before they are admitted for surgery. The clinical team completes the patient assessment, prepares the patient for the transplant, and performs the procedure. Patient management and monitoring for the perioperative period is supported by the following personnel:

-) RN and APN, Cardiologist
-) Surgical team
-) CCCU/ICU
-) Administrative support

In addition to the recommendations below, all transplant hospitals are expected to have their own protocols on how to treat complications common to surgery and heart failure patients. Each program has expertise in transplantation, advanced heart failure management and the flexibility to consult with other medical specialties and multidisciplinary teams to inform complex care practices beyond the scope of existing recommendations.

Consultations	
Anaesthesia	one time
Transplant education & clinical trials	one time
Cardiology	one time
Surgical	one time

Laboratory Testing	
CBC	one time
Electrolytes	one time
PT, PTT, INR	one time
Type and Screen	one time
Crossmatch	one time
Isohemagglutinins (if ABO incompatible)	one time
Total bilirubin, Bilirubin, Albumin, Total Protein, ALP, AST, ALT, GGT	one time as needed

Imaging	
Chest X-Ray	one time
ECG	one time as needed

Treatment	
Peripheral IV insertion	one time

Transplant Surgery

Preoperative assessment and monitoring by surgical team

Transplant surgery including transplant surgeon, surgical team, anesthesiologist, operating room staff, and all other resources required during the surgery.

Immediate post-transplant monitoring and management

Post-Anesthetic care (recovery phase)

Post-operative care unit

Diagnostic and laboratory assessment

Paediatric Post-Transplant: During Hospital Admission

Clinical Care: Transplant programs are responsible for patient management during the post-transplant phase, hospital admission phase. During this phase, clinical teams continue to monitor patients, administer pain medication, and ensure necessary testing and interventions are completed. Patients will initially be monitored in the intensive care unit before being transferred to the surgical ward. Patients also begin their immunosuppression therapy. Ongoing patient management, monitoring, education and nursing care is supported by the following personnel.

-) RN and APN, MD
-) Allied health care (social work, physiotherapy, occupational therapy, pharmacy, and nutrition)
-) Administrative support

In addition to the recommendations below, all transplant hospitals are expected to have their own protocols on how to treat complications common to all transplant and heart failure patients. Each program has expertise in transplantation, advanced heart failure management and the flexibility to consult with other medical specialties and multidisciplinary teams to inform complex care practices beyond the scope of existing recommendations.

Consultations

Patient education	ongoing
Dietitian	ongoing
Physiotherapy	ongoing
Pharmacy	ongoing
Transplant Coordinator	ongoing

Imaging

ECG	one time
Echo	<ul style="list-style-type: none"> • day 1 or 2 • weekly to 2 months

Treatment

Pacer Wires (dressing and removal)	one time
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Infectious Disease

CMV PCR	at least once
EBV PCR	at least once

Laboratory Testing

CBC	daily
Electrolytes	daily
Total bilirubin, Bilirubin, Albumin, Total Protein, ALP, AST, ALT, GGT, Glucose	daily
Urea, Creatinine	daily
PT, PTT, INR	daily
Immunosuppression levels	as needed
Isohemagglutinins (if ABO incompatible)	daily for 5 days, then weekly

Other tests/Assessments

Heart Biopsy	7-21 days for first biopsy, then as needed
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Paediatric Post-Transplant: After Discharge

Clinical Care: Transplant programs are primarily responsible for patient management during the post-transplant phase after discharge from the hospital. The transplant team and appropriate health care providers monitor patients through outpatient clinic visits, ensure the necessary testing is completed, interpreting laboratory and diagnostic results and collaborating with other members of the multidisciplinary transplant team as required. The transplant program also monitors and adjusts immunosuppression therapy to prevent organ rejection. Ongoing management and monitoring of the patient's transplant is completed by the transplant program and is supported by the following personnel.

-) RN and APN, MD
-) Allied health care (social work, physiotherapy, psychology, occupational therapy, pharmacy, and nutrition)
-) Administrative support

Paediatric patients will be transitioned to an adult transplant centre at age of 18 years. Each program has expertise in transplantation, advanced heart failure management and the flexibility to consult with other medical specialties and multidisciplinary teams to inform complex care practices beyond the scope of existing recommendations.

Consultations	
Transplant education	ongoing as needed
Physiotherapy/ Rehabilitation	first 3 months, then as needed
Social work	ongoing as needed
Adolescent medicine	at age 11 years then annual
Neurodevelopmental assessment	6 and 12 months post-transplant and preschool
Neuropsychologist	as needed
Dietician	ongoing as needed

Infectious Profile	
CMV PCR	<ul style="list-style-type: none"> • weekly for 1 month • weekly-q2 weeks: 3 months • Monthly: 6-12 months • q3-6 months: 1 year, then as needed
EBV PCR	<ul style="list-style-type: none"> • weekly for 1 month • weekly-q2 weeks: 3 months • Monthly: 6-12 months q3-6 months: 1 year, then as needed
Varicella	• annual
Hep B Titres	• 6-12 months following immunization

Laboratory Testing	
Electrolytes, urea, magnesium, creatinine, GFR, glucose	<ul style="list-style-type: none"> • weekly for 1 month • weekly-q2 weeks: 3-6 months • q2 weeks-Monthly: 6-12 months • q3-6 months: ≥ 1 year, then as needed
CBC	<ul style="list-style-type: none"> • weekly for 1 month • weekly-q2 weeks: 3 months • monthly: 6-12 months • q3-6 months: ≥ 1 year, then as needed
Liver Function Tests	q3-6 months or as required
Lipid levels	one time at 3 months, then q6-12 months
Hgb A ₁ C for diabetic patients only	q6 months, and as needed
PTH	q6 months > 1 year
25(OH) Vit D	q6 months > 1 year
Urinalysis	q6 months > 1 year
Urine albumin/creatinine ratio	q6 months > 1 year

Services continued on next page

Paediatric Post-Transplant: After Discharge

Continued from previous page

Immunologic Evaluation	
Immunosuppression Levels	<ul style="list-style-type: none"> • weekly for 1 month • weekly-q2 weeks: 3-6 months • q2 weeks-monthly: 6 -12 months • q3-6 months: ≥1 year
HLA antibody screen and antibody specificities	Qbiopsy and/or q3 months x 1 year then annually
Isohemagglutinins <i>for ABO incompatible patients only</i>	<ul style="list-style-type: none"> • weekly for 1 month • q2 weeks to 3 months • monthly to 6 months • q3 months to 1 year • 3-6 months >1 year

Imaging	
ECG	annual (with holter)
Bone Mineral Density	Age 5 years, then q5 years unless abnormal
Non-invasive stress tests	q2 years
Coronary angiography/intravascular ultrasound	5 and 10 years, then as needed
Holter Monitor	annual (with ECG)
Echo	<ul style="list-style-type: none"> • weekly to 2 months • Q2 weeks to 3 months • Q4 weeks to 6 months • Q8 weeks to 1 year Long-term: 2-3 per year
24 hour ambulatory blood pressure monitoring (ABPM)	<ul style="list-style-type: none"> • 6 months if hypertensive or on antihypertensive medications, otherwise 1 year. • Annual if decreased renal function, on maintenance steroid, sirolimus, and/or antihypertensives. Biennially if normal renal function

Other Tests/ Assessments	
Heart Biopsy	<ul style="list-style-type: none"> • q3-8 weeks: 1-6 months • q8-16: 6-12 months • q4-12 months: 1-3y • q6-12 months: 3-5y thereafter as needed

Quality of Life	
CHQ-CF/PF	annual
PedsQL 4.0	Parent/guardians of recipients 2-17 years of age
QOLVAS	annual

IX. Implementation

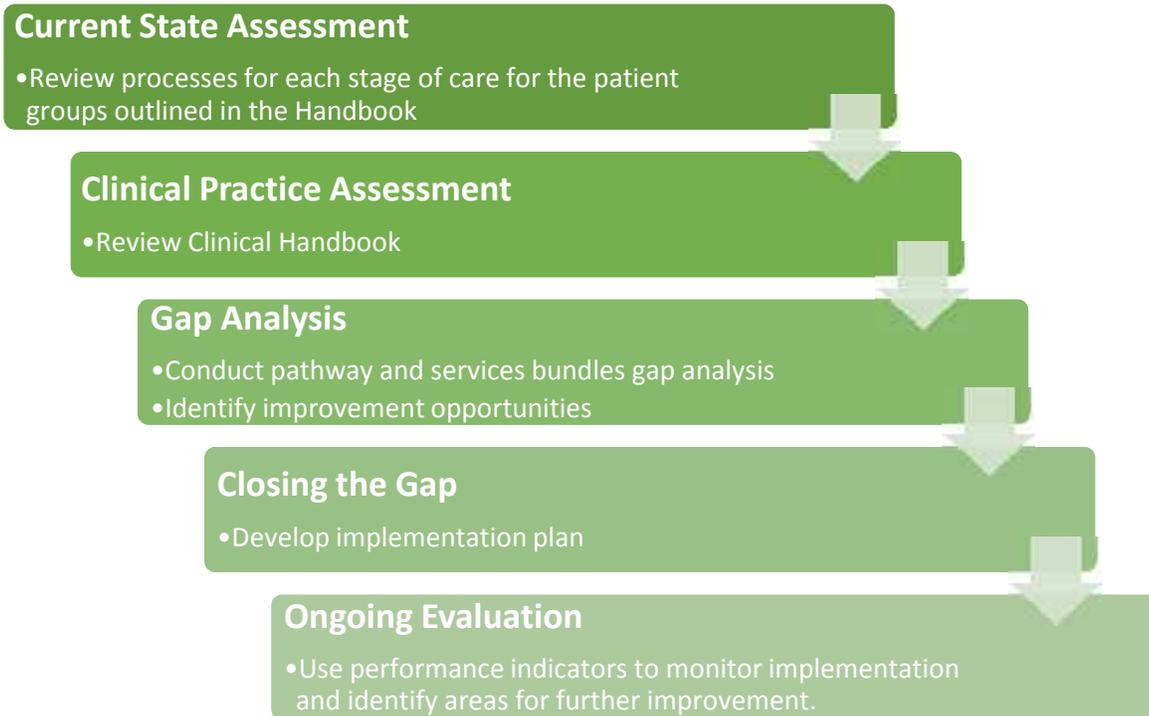
The Clinical Handbook is a compendium of evidence-based and clinical consensus guidelines created with the goal of improving quality of transplant care delivery and patient outcomes as measured through performance indicators. This toolkit is not intended to replace the professional skill and judgement of healthcare providers, nor inhibit the development of new and innovative transplant solutions.

Successful implementation of the Handbook can be facilitated by leveraging the following components:

-) **Building a shared vision for clinical practice:** The Clinical Handbook is an opportunity to share clinical consensus guidelines that will allow the system to provide even better quality care, while increasing system efficiencies.
-) **Engaging leadership for change:** Senior leaders can support the vision for change by providing a clear message about the implications of guideline implementation.
-) **Supporting clinical engagement:** From the outset, staff, physicians and other clinicians should be provided with sufficient information that will help them understand the importance of this initiative, including its impact on patient care.

To achieve a shared vision for clinical practice, transplant centres are encouraged to review their current processes in relation to the clinical pathway and identify any variation that exists. As transplantation is a complex system, when a variation is identified, transplant centers are encouraged to work within their centers to understand the variation in developing their local clinical pathway. To help with the review process the following roadmap to implementation has been suggested.

Roadmap to Heart Transplant Clinical Pathway and Service Bundles Implementation



The Clinical Handbook provides an opportunity to build a shared vision for clinical practice for heart transplantation to improve quality of care, while maximizing the effective use of available resources. In order to make informed and accurate decisions, the importance of high-quality data cannot be emphasized enough. As outlined in section III, TGLN has developed a list of quality indicators that can be used to evaluate each stage of the patient care continuum. Such indicators will enable centres to track, audit, and evaluate the implementation of the clinical pathway and service bundles at an organizational level. Through such monitoring, variances can be identified, progress monitored, and practices refined over time to improve patient outcomes.

The Heart and Lung Working Group will utilize performance metrics to review clinical practices and make recommendations to support practice changes where notable variations in practice have been identified. The Clinical Handbook will be reviewed regularly by the Working Group and when appropriate, updated with new recommended practices, evidence, and policy changes.

X. References

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XI. Appendices

Appendix A. Adult Heart Transplantation Referral & Listing Criteria

PATIENT REFERRAL CRITERIA:

The patient referral criteria are guidelines which a Health Care Provider would utilize to refer a patient to a transplant center for assessment. The criteria identified below are the conditions for which a patient should be referred for heart transplant assessment.

- 1) **Advanced Heart Failure:** Referral for heart transplantation should be considered for patients with advanced heart failure failing optimal medical and surgical (if appropriate) therapy. Such patients would have one or more of the following:
 -) Late-stage heart failure due to any cause [American Heart Association (AHA) stage D];
 -) Patients who have significant cardiac dysfunction with marked symptoms of dyspnea, fatigue end-organ hypoperfusion at rest or with minimal exertion despite maximal medical therapy and/or surgical therapy; or,
 -) Refractory symptoms requiring specialized interventions to manage symptoms or prolong life.
- 2) **Anticipated Survival:** Referral for heart transplantation should be considered for patients with poor anticipated survival without a transplant.
- 3) **Quality of Life:** Referral for heart transplantation should be considered for patients who would experience an unacceptable quality of life without a transplant.
- 4) **Arrhythmias:** Referral for heart transplantation should be considered for patients who have refractory life-threatening arrhythmias despite optimal medication, surgical, and device therapy.
- 5) **Heart Disease:** Referral for heart transplantation should be considered for patients with complex congenital heart disease with failed surgical palliation or who are not amenable to surgical palliation at acceptable risk.
- 6) **Angina:** Referral for heart transplantation should be considered for patients with refractory angina not amenable to further revascularization.

Early referral is essential, allowing for pre-transplant problems to be addressed and resolved while the disease is relatively well-compensated.

PATIENT LISTING INDICATIONS:

Each patient is assessed individually for their suitability for heart transplantation by the transplant program. The criteria identified below are the conditions for which a patient may be eligible to be waitlisted for heart transplantation in Ontario.

- 1) **Advanced Functional Class:** Patients considered Class III to Class IV (severe) according to the New York Heart Association (NYHA) functional classification system may be considered for transplant listing. Listing for heart transplant may also be considered for patients who have refractory life-threatening arrhythmias that are not amenable to treatment.
- 2) **Functional Capacity – Poor One Year Survival:** Patients with functional capacity resulting in poor expected one year survival may be listed for transplant. Such patients would meet the following criteria:
 -)] An absolute indication for listing includes patients with a peak VO_2 of less than 10 mL/kg/min with achievement of the ventilatory threshold. Relative listing indications include patients with peak VO_2 between 11 mL/kg/min and 14 mL/kg/min or less than 55% of the predicted value for the age group.
 -)] Listing may be considered for patients with a peak VO_2 of 15 mL/kg/min or greater to 18 mm/kg/min or less with refractory angina or life-threatening arrhythmia. For patients treated with beta blockers, the threshold for transplantation should be lowered to less than 12mL/kg/min.
- 3) **Lack of Alternative Medical Options:** Patients who fail to respond to maximal medical therapy or the absence of alternative/conventional surgical options are eligible to be waitlisted for heart transplantation in Ontario.
- 4) **Contraindications:** The absence of contraindication(s) for transplant is required to be eligible to be wait-listed for heart transplantation.
- 5) **Rehabilitation:** The potential to undergo rehabilitation after transplant is required to be eligible to be wait-listed for heart transplantation.

ABSOLUTE LISTING CONTRAINDICATIONS:

The following are conditions relating to the heart transplant candidate that constitute absolute contraindications to heart transplantation. As such, they prevent a transplant from being done until the condition is resolved.

- 1) **Liver Disease:** Patients with advanced primary liver disease are not candidates for heart only transplantation, but may be considered for combination heart-liver transplantation.
- 2) **Pulmonary Hypertension (PHT):** Patients with irreversible pulmonary arterial hypertension should not be considered for transplantation, but should be considered for advanced therapies to treat PHT.
- 3) **Malignancy:** Patients with recent active malignancy are not candidates for heart transplantation but may be considered for transplant when tumor recurrence is low based on tumor type, response to therapy, and negative metastasis work-up.
- 4) **Pulmonary Disease:** Patients with irreversible pulmonary parenchymal disease are not candidates for heart transplantation. Lung function should be assessed after optimal medical therapy for heart failure has been achieved. Candidates with a FEV_1/FVC ratio of less than 40% to 50% of predicted, or FEV_1 less than 50% of that predicted despite optimal medical management for heart failure are poor candidates for transplantation.

- 5) **Consent:** Patients who do not want a transplant should not be listed for heart transplantation. Patients who are unable to give informed consent and do not have a substitute decision maker available, resulting in an inadequate or unsafe care plan post-transplant, are not candidates for heart transplantation.
- 6) **Systemic Disease:** Patients with primary systemic disease limiting long term survival are not candidates for heart transplantation (e.g. hepatic disease).
- 7) **Infections:** Patients should be free of active infection, whether of viral, bacterial or fungal origin. Patients with active AIDS are not candidates for transplantation.
- 8) **Psychosocial Considerations:** Patients must undergo a complete psychosocial evaluation prior to listing for transplant. Patients who display the following are not candidates for heart transplantation:
 1. Drug or alcohol abuse (3 months abstinence is required and willingness to enter a structured rehab program);
 2. Patients with severe cognitive-behavioural disabilities or dementia;
 3. Psychiatric condition (unstable or chronic) leading to reduced chance of successful transplant due to compliance considerations;
 4. Documented life threatening non-compliance; or,
 5. Active smoking (3 months abstinence is required).

RELATIVE LISTING CONTRAINDICATIONS:

The following are conditions relating to the heart transplant candidate that constitute relative contraindications to heart transplantation. While each patient is evaluated on an individual basis, the presence of one or more of the following may preclude a candidate from being listed on the heart transplantation wait list.

- 1) **Age:** Patients with advanced age may not be eligible for heart transplantation.
- 2) **Pulmonary Hypertension:** Patients with a pulmonary vascular resistant (PVR) exceeding 5 Wood units may not be eligible for heart transplantation.
- 3) **Osteoporosis:** Patients with severe osteoporosis, with bone mineral density >2 standard deviations (SD) below normal or at high risk may not be eligible for heart transplantation.
- 4) **Obesity:** Patients with morbid obesity and a body mass index (BMI) of >35 kg may not be eligible for heart transplantation.
- 5) **Diabetes:** Patients with diabetes with end organ damage may not be eligible for heart transplantation (e.g. neuropathy, nephropathy and retinopathy).
- 6) **Gastrointestinal Disease:** Patients with active peptic ulcer disease may not be transplanted until the disease is successfully treated. Patients with active diverticulitis may not be candidates for heart transplantation.
- 7) **Cachexia:** Patients with marked Cachexia ($< 60\%$ of ideal body weight) may not be eligible for heart transplantation.
- 8) **Functional Capacity:** Patients with a peak VO_2 (oxygen consumption) higher than 15 mL/kg/min without other indications for transplantation (excluding congenital cases) may not be eligible for heart transplantation.
- 9) **Pulmonary Infarction:** Patients with recent unresolved pulmonary infarction may not be eligible for heart transplantation.

- 10) Technical Issues:** Patients who are surgically unsuitable, where a successful transplant is unlikely due to surgical risks/technical issues (e.g. excessive scar tissue in chest from previous cardiac surgeries), may not be eligible for heart transplantation.
- 11) Peripheral and Cerebral Vascular Disease:** Patients with severe peripheral and/or cerebrovascular disease may not be eligible for heart transplantation when its presence limits rehabilitation and revascularization is not a viable option.
- 12) Renal Dysfunction:** Patients with irreversible or primary renal dysfunction and a serum creatinine > 200µmol/L after inotropic challenge and adjustment of medications may not be eligible for heart transplantation.
- 13) Amyloidosis:** Patients with primary or secondary amyloidosis may not be eligible for heart transplantation.
- 14) Cardiac Disease:** Patients with myocardial infiltrative and inflammatory disease may not be eligible for heart transplantation.
- 15) Social Support:** Patients for whom social supports are deemed insufficient to achieve compliant care in the outpatient setting.

GENERAL CONSIDERATIONS:

In addition to the above criteria, the following should be considered when assessing candidates for heart transplantation.

- 1) Human Leukocyte Antigen (HLA) Sensitization:** Transplantation of sensitized recipients is associated with significant risk for early graft failure and reduced survival as a result of humoral rejection. Recognition and measurement of the degree of sensitization to HLA antigens is an important part of the evaluation of transplant candidates.

Appendix B. Adult Heart Transplant Referral Form

Referral Criteria for Heart Transplantation:

- 1) **Advanced Heart Failure:** Referral for heart transplantation should be considered for patients with advanced heart failure failing optimal medical and surgical (if appropriate) therapy. Such patients would have one or more of the following:
 -) Late-stage heart failure due to any cause- AHA stage D
 -) Patients who have significant cardiac dysfunction with marked symptoms of dyspnea, fatigue end-organ hypoperfusion at rest or with minimal exertion despite maximal medical therapy and/or surgical therapy
 -) Refractory symptoms requiring specialized interventions to manage symptoms or prolong life.
- 2) **Anticipated Survival:** Referral for heart transplantation should be considered for patients with poor anticipated survival without a transplant.
- 3) **Quality of Life:** Referral for heart transplantation should be considered for patients who would experience an unacceptable quality of life without a transplant.
- 4) **Arrhythmias:** Referral for heart transplantation should be considered for patients who have refractory life-threatening arrhythmias despite optimal medication, surgical, and device therapy.
- 5) **Heart Disease:** Referral for heart transplantation should be considered for patients with complex congenital heart disease with failed surgical palliation or who are not amenable to surgical palliation at acceptable risk.
- 6) **Angina:** Referral for heart transplantation should be considered for patients with refractory angina not amenable to further revascularization.

To refer a candidate for heart transplantation, complete this form and attach all applicable documents.

Please indicate if your patient needs an URGENT or STANDARD assessment.

Submit the completed form, including all applicable documents to the appropriate transplant centre listed below:

Toronto General Hospital
Heart Function Clinic
Norman Urquhart Building, 5th Floor
585 University Ave.
Toronto, Ontario M5G 2N2
Fax: 416 340 4134

London Health Sciences Centre
Multi-Organ Transplant Program
339 Windermere Road
London, Ontario, N6A 5A5
Fax: 519 663 3858

University of Ottawa Heart Institute
Heart Transplant Program
40 Ruskin Street
Ottawa, Ontario K1Y 4W7
Fax: 613 761 4327

The completion of this form will expedite your patient's investigations and subsequent consideration for transplantation. Thank you for your cooperation in providing this material.

ADULT HEART TRANSPLANTATION REFERRAL FORM

Referral Type: URGENT STANDARD

Referring MD: _____ Contact #: _____

Referring Centre: _____ Postal Code: _____

Referral Form submitted to: _____ Date Submitted: _____ Date received: _____

PATIENT DEMOGRAPHIC INFORMATION

Patient Name: _____ Health Card #: _____

Date of Birth: _____ Sex: Male Female Unknown

Address/City: _____ Postal Code: _____

Language Spoken: _____

PATIENT CARDIAC INFORMATION

Patient ABO (attach report): _____ Height: _____ Weight: _____

Diagnosis: _____ New Referral? Yes No (re-transplant)

Baseline Characteristics:

EF _____ % / grade _____

NYHA Class: 1 2 3 4

BP: _____

QRS > 120 ms: Yes No

Devices: Yes No

Biv Pacer: Yes No

Biv AICD: Yes No

AICD: Yes No

Laboratory Data:

Hb _____ Uric Acid: _____ Na: _____

% Lymphocytes _____ Total Cholesterol: _____ Creatinine: _____

NT proBNP (optional): _____

Medications:

Lasix _____ mg (od bid tid)

Metalozone _____ mg (od bid)

HCTZ _____ mg od

ACEI: Yes No

Beta-blocker: Yes No

ARB: Yes No

Allopurinol: Yes No

Statin: Yes No

Aldosterone blocker: Yes No

LAB RESULTS

Please attach the copies of the following reports, WHERE APPLICABLE:

- 2D echocardiogram Abnominal Ultrasound Angiogram and CD Chest x-ray
 Bone Density Scan CT Scan of Chest ECG Urine Tests
 Blood Test Results Heart Stress Tests Hemodynamic Monitoring

PAST MEDICAL HISTORY

History of cancer:

- No Yes, please explain: _____

History of peripheral vascular disease (ie., carotid, AAA, PVD):

- No Yes, please explain: _____

Past surgeries:

- No Yes, please explain: _____

History of psychiatric conditions (ie., social support, current substance abuse):

- No Yes, please explain: _____

History of neurological conditions (ie., stroke and associated deficits):

- No Yes, please explain: _____

COPD or lung related problems:

- No Yes, please explain: _____

Please include any past medical history that may be relevant to patient assessment:

REFERRING CARDIOLOGIST

Patient Referral Type: Outpatient Inpatient

Referral letter attached

Name: _____ Phone #: _____

Signature: _____ Date: _____

To be completed by Transplant Cardiologist:

Urgency: High Average

Name: _____ Signature: _____ Date Received : _____