A REPRODUCIBLE AND STANDARDISED CLINICAL REGISTRY FOR CLINICAL AND ECONOMIC OUTCOMES OF HEART TRANSPLANTATION PATIENTS

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Abstract

This study describes the creation and implementation of a prospective, reproducible and standardised clinical registry of outpatients who underwent heart transplantation. Methods and Results: The following steps were carried out: i) data were standardised in accordance with national and international standard data elements, ii) an initial data collection and clinical research workflow was developed, iii) electronic case reports were developed in accordance with the HIPAA privacy rule using REDCap, iv) pilot testing and validation of the data collection, clinical research workflows and case report forms was undertaken, and v) an automated data quality report was developed using REDCap. All patients undergoing heart transplantation in a reference cardiology hospital were included. Patients were excluded if they did not agree to participate in the study. The registry was designed to become multicentre in the future. Data were collected from the moment of the inclusion (hospital admission), at hospital discharge, and 1, 3 and 6 months and yearly after surgery. Clinical and cost-related outcomes included all-causes mortality, cardiovascular mortality, non-fatal myocardial infarction, stroke, hospital admissions, visits to the emergency department, organ rejection, infection, need for re-operation, any adverse event, costs related to treatment and procedures, and quality of life. Conclusions: This registry represents a powerful tool for assisting quality improvement, healthcare services management, technology assessment, health policies and clinical research since it contains comprehensive and representative data of the clinical practice and allows for interoperability and data integration with other datasets.

Keywords: heart transplantation; quality indicators; registries; Brazil

Introduction

Chronic heart failure (CHF) is a public health issue due to its high prevalence and mortality.[1-3] In its terminal stage, CHF incurs high costs due to onerous treatment and high re-admission numbers. With the passing of years and treatment advances, mortality has declined, with heart transplantation considered as the golden treatment for refractory CHF.[2-4] Cardiac transplantation needs specialised personnel and organisational structures and studies to improve care of these patients care are still needed.[3]

To achieve this, it is important to improve the quality of data collected on these patients. This paper describes the creation and development of a clinical registry of outpatients who underwent a cardiac transplant at the Cardiology Institute of RS – Cardiology University Foundation (IC-FUC).

Methods

In June 2015, a prospective study was undertaken to design a Clinical Registry for IC-FUC that could be expanded to other centres. Development of the registry went through four stages, variable standardisation, REDCap software implementation, development of a case report form (CRF), and registry implementation. As a pilot test to evaluate the functionality of the registry, data of all patients who had undergone a cardiac transplant at the Cardiology Institute assembly were entered.

REDCap software was chosen as it is recognised for its safety and applicability for data collection and storage, and compliance with the Health Insurance Portability and Accountability Act (HIPAA) guidelines.[6] A license for its use was obtained from Vanderbilt University.

Variable standardisation To standardise the variables, data elements related to cardiac transplantation were

evaluated and selected from documents from national[3] - Brazilian Cardiology Association, and international - American Heart Association,[2] International Society for Heart and Lung Transplantation (ISHLT4),[5] associations and societies.

To facilitate interoperability among datasets and the exchange of information in a fast and precise way the Registry of Transplant aimed to use similar variables to those used by ISHLT, a world acknowledged registry. Some of the similar variables are shown in Table 1.

A dashboard was created to display patient data over time. This includes periodic patient examination and assessment, evaluation of the treatment, the functional state of the patient as well as rejection occurrence and treatment choice. This can be used to study and evaluate the institution's experience and select the most effective care based on outcome. The dashboard also allows double-checking and verification of data entered. (Figure 1)

The structure of the case report form was developed is shown in Table 2 and the electronic CRF was then developed in REDCap.

Progress and quality report and bias prevention

Data quality rules are established within REDCap and data quality control occurs through several strategies. (Figure 2)

Data quality reports are automatically generated every month using REDCap. This allows early identification of errors, exemplified by unfilled fields, or problems related to inconsistent information such as observing implausible values. The electronic CRF also prevents incomplete data entry, and test results values outside of plausible biological ranges.

Ethical considerations and responsibilities

This clinical study was conducted in accordance with the principles of the current revision of the Helsinki Declaration and the Clinical Good Practice Guidelines (ICH-GCP) in its latest version and Resolution 466/12.

Table 1. Examples of similar variables used in the Cardiology Institute Registry and the ISHLT Registry.

Variables from our Cardiac Transplants Registry	ISHLT Variables
Patient ID	Patient ID
Birth date	Birth date
Patient gender	Patient gender
Race	Race
Previously IAM	Previously IAM
Primary diagnosis for transplant	Primary diagnosis for transplant
Medical History of Diabetes prior to transplant	Medical History of Diabetes prior to transplant
Donor Cause of Death:	Donor Cause of Death:
Biological or Anti-viral Therapy:	Biological or Anti-viral Therapy:

Source: IC-FUC Cardiac Transplants Register. Available at: http://redcap.cardiologia.org.br/redcap/redcap_v7.0.0/ProjectSetup/index.php?pid=78. ISHLT Register. Available at: http://ishlt.org/registries/heartLungRegistry.asp.

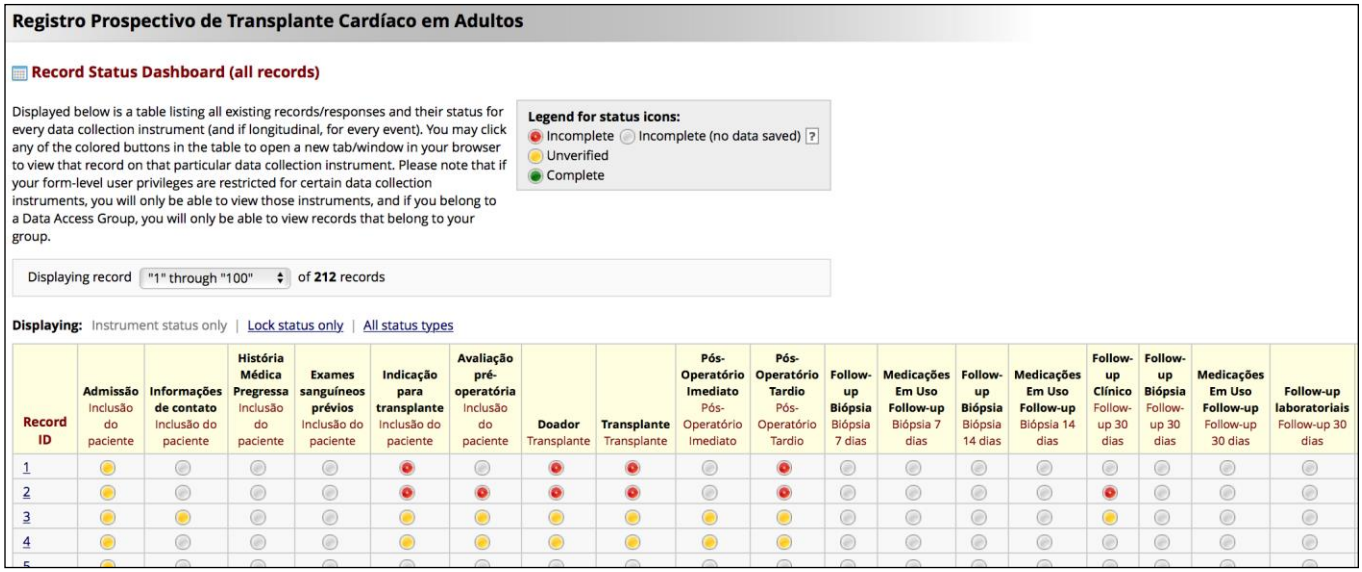

Figure 1. Record status dashboard. Source: REDCap IC-FUC. Available at: http://redcap.cardiologia.org.br/redcap/redcap_v7.0.0/ProjectSetup/index.php?pid=78

Table 2: Standardised variable session.

Instrument name	Variable Class
Admission	Patient ID; medical record register; birth date; age; list entry data; transplant patient age; blood type; schooling; job before transplant; race; sex.
Contact information	Address; main phone; secondary phone; familiar phone; e-mail.
Previous Medical History	Presence or not of : hypertension, dyslipidaemia, embolic event, cancer, smoking record, renal insufficiency, psychiatric disease, family history of cardiomyopathy; rheumatic disease; arrhythmia; ventricular arrhythmia; atrial fibrillation or flutter; cerebrovascular disease; previous CVA, peripheral vascular disease; cardiovascular surgery; previous blood transfusion; infection with antibiotic treatment; previous gestation; familiar history of CAD; peptic ulcer; ex-alcoholic; hepatic insufficiency; amyloidosis; sarcoidosis; previous angioplasty; use of electronic cardiac dispositive; continuous-use medication
Previous blood exams	Virology; blood exam; gasometrical; renal function; liver function; anticoagulation.
Transplant Indication	Diagnosis data; which primary dispositive for transplant; list time.
Pre-operative evaluation	Weight; height; immunological panel; INTERMACS; pre-operatory condition; clinical condition; life support use, drugs use (vasoactive); functional status before transplant, pre-transplant physical capacity; previous ejection fraction; catheterisation; ECG; RX, electrocardiogram; vasoreactivity test; ergoespirometry.
Donor data	Donor hospitalisation place; encephalic death confirmation time; sex; weight; age; death mechanism; cause of death; blood type; border donor; previous RCP; MD; insulin dependent; HAS; cancer; Chagas history; tuberculosis history; blood infusion administration; medications in use, smoking data; alcoholic; laboratorial exams (renal function, virology); use and dose of vasopressor; vital signs previous to transplant; cross-match; ALH; in culture confirmed presence of infection
Transplant	Procedure time; organ withdrawal time; utilised solution to preservation of graft; beginning and end time of transplant; chosen technique for implant; time of ischemia; time of clamp; use of vasopressors or adrenergic intrasurgery; necessary use of post-surgery peacemaker; presence of clinic important events (bleeding, arrhythmia, low debt syndrome); graft acute dysfunction; ventilator or renal dysfunction; intraoperative death occurrence
Immediate Post-operative	Crystalloid balance, blood balance; initial and final haematocrit; RASS; diuresis; occurrence of hemodynamic instability and applied behaviour; presence of hyperacute rejection and medication used; medication chosen to maintain immunosuppression; occurrence of death.
Late Post-operative	Need for reoperation; prolonged MV; renal failure; Hepatic dysfunction; antiviral therapy in use; biopsy and results; immunosuppressive drugs in use; death.
Clinic Follow-up	Death; weight; post-transplant functional status; vaccine schedule; re-admission; MD; SAH; dyslipidaemia; VTE / PE; atrial fibrillation; EVA; non-fatal RCP; exams after transplantation.
Biopsy Follow-up	Date of examination; presence of humoral or cellular rejection; antibody found; other findings on the biopsy.
Follow-up use medicatio	Medications in use after transplantation (ARB, ACE inhibitors, diuretics, statins, antiplatelet agent, anticoagulant, non-cardiovascular drugs, immunosuppressive medication)
Laboratory Follow-up	Haemogram; renal function; liver function; virology

ECG: Electrocardiogram; MD: Mellitus Diabetes; COPD: Chronic Pulmonary Obstructive Disease; CAD: Coronary Artery disease; SAH: Systemic Arterial Hypertension; PTCA: Percutaneous Transluminal Coronary Angioplasty; CVA: Cerebrovascular Accident; AF: Atrial Fibrillation; RCP: Cardiorespiratory Arrest; HLA: human leukocyte antigen; RASS: Richmond Agitation Sedation Scale; INTERMACS: Interagency Registry for Mechanically Assisted Circulatory Support; MV: Mechanical ventilation; VTE: venous thromboembolism; PE: Pulmonary embolism, Inhibitors ACE: angiotensin converting enzyme inhibitors; ARB: angiotensin receptor blockers
Source: REDCap IC-FUC. Available at: http://redcap.cardiologia.org.br/redcap/redcap_v7.0.0/ProjectSetup/index.php?pid=78

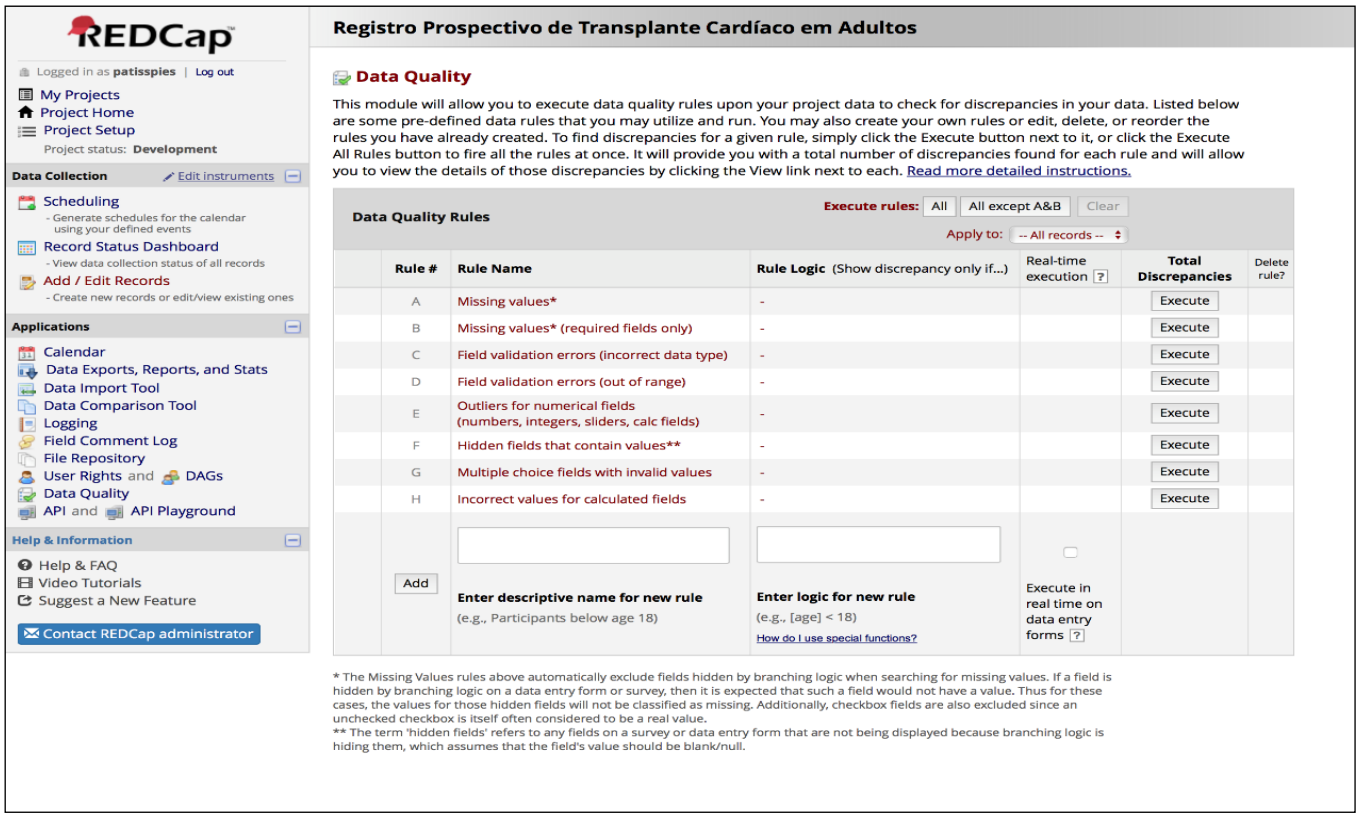

Figure 2. Setting up data quality rules.

It is also be carried out obeying the local legal and regulatory requirements of Brazil. The Institutional Review Board (IRB) of IC-FUC approved all submitted protocols, forms, as well as the Informed Consent Term and the Data Responsibility Term (used for previously transplanted patients).The names of all patients are kept confidential; they are identified in the documentation and during the assessment, by the number assigned to each of them in the study. All findings are stored on computer and handled in the strictest confidentiality rules to assure the patients.

Conclusion

Through collected information in the database, the Registry of Cardiac Transplant provides the opportunity for new studies and improved care of patients who have undergone a cardiac transplantation. The generation of high quality and comprehensive data allows high impact research to be conducted generating competitive scientific publications at the national and international level. In addition, these data can support a number of other future studies, deepening the knowledge of studied areas.

Regarding the technological approach, clinical records represent the most appropriate way of evaluating products and processes implemented in clinical practice, by gathering sequential information from a large number of patients; in this way, it is possible to both evaluate current technologies and identify the need to improve them in order to create new products and processes.

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