Centre universitaire de santé McGill

McGill University Health Centre

ANNUAL REPORT 2017-18

Technology Assessment Unit of the McGill University Health Centre

Email: Nandini.dendukuri@mcgill.ca
Website: www.muhc.ca/tau
Tel: 514-934-1934 x 36916

Centre for Outcomes Research and Evaluation
5252 boul. de Maisonneuve, 3F.50
Montreal, Quebec, H4A 3S5

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MANDATE

Mission Statement

- To advise the hospital in difficult resource allocation decisions, using an approach based on sound, scientific technology assessments, and a transparent, fair decision-making process.
- To publish its research in peer-reviewed journals when appropriate, and contribute to the training of personnel in the field of health technology assessment.

Vision

Using the best available scientific evidence, TAU aims to aid in the delivery of quality health care, and the efficient utilization of medical resources.

"Doubt is not a pleasant condition, but certainty is an absurd one."
Voltaire (1694 - 1778)

TAU COMPOSITION

The TAU is composed of a scientific research staff, and an inter-disciplinary policy committee representing physicians, nurses, allied health professionals and patients.

Policy Committee

Nandini Dendukuri	**TAU Director**
James Brophy	**Chairperson**
Maurice McGregor	**Chair Emeritus**
External committee members	Discipline
André Bonnici	Pharmacy & Therapeutics
Christos Calaritis	Multidisciplinary Council
Todd Lee and Emily McDonald	Council of Physicians and Dentists
Patricia Lefebvre & Teresa Mack	Quality, Risk Management & Performance
Brenda MacGibbon-Taylor	Patients' Committee
Nancy Mayo	Division of Clinical Epidemiology
Alyson Turner	Council of Nurses

Research Staff

Nisha Almeida	Research Scientist
David Felipe Forero	Research Assistant
Lorraine Mines	Administrative Technician
Alain Lapointe	Consultant

TAU REPORTS

NOTE

Projects are researched and drafts prepared by the research staff of the MUHC TAU, referred to below as "the authors". They are assisted by expert consultants appointed for each project. Draft reports are then circulated, reviewed, amended and finally approved by the full TAU Policy Committee who thereby take ownership of the recommendations made.

DIFFUSION

- Our reports are indexed in the international database for the Center for Reviews and Dissemination, York University, UK: http://www.crd.york.ac.uk/CRDWeb/
- Our reports are diffused from our website: www.muhc.ca/tau

The following reports were completed this year, and are described in greater details in the following pages:

Use of Extracorporeal Membrane Oxygenation for Cardiac Life Support in adult subjects

Title

Use of Extracorporeal Membrane Oxygenation for Cardiac Life Support in adult subjects

Requestor

Dr. Peter Goldberg, Intensive Care Unit

Publication Date

June 26, 2017

Authors

Nisha Almeida, Lama Saab and Nandini Dendukuri

Background

Extracorporeal membrane oxygenation (ECMO) uses the creation of an external blood gas exchange circuit to provide temporary life support to patients in acute respiratory or cardiac failure, and includes veno-venous (VV) ECMO and veno-arterial (VA) ECMO. When VA-ECMO is used during cardiopulmonary resuscitation, it is known as ECPR. ECMO has a long history of use to support neonates in respiratory failure. ECMO use in adults has greatly increased since 2010, with expanding cardiac failure indications.

Conclusions

- ECMO is a temporary life support technique to support patients with acute heart or respiratory failure and high risk of mortality. Since 2010, ECMO use in adults has increased, and indications have expanded to adults in cardiac failure.
- Given the limited evidence base, it remains unclear whether VA-ECMO prolongs survival and results in better neurological outcomes relative to alternative treatments such as ventricular assist devices, cardiopulmonary bypass and mechanical ventilation. Data from comparative studies suggest some evidence of improved survival with ECPR relative to conventional CPR. However, ongoing RCTs of ECPR vs conventional CPR in cardiac arrest patients indicate continued equipoise VA-ECMO in adult cardiac patients xvi June 26, 2017 Technology

Assessment Unit, MUHC for trials of ECMO in this population. Data from case series indicate that survival to discharge after VA-ECMO for cardiogenic shock is approximately 40%.

- Although some organizations have attempted to develop guidelines for indications of ECMO use, the current literature has not established clear normative guidelines due to the heterogeneous study population and limited body of evidence on clear indicators for survival.
- Recent evidence suggests that patients receiving ECMO at high-volume centres (>30 adult ECMO cases per year) have lower mortality rates than those treated at centres with fewer than six adult cases annually, making the case for concentrating ECMO treatment in a few high-volume centres.
- At the MUHC, 41 adults have been supported with ECMO since 2013. Survival was comparable to data reported in large case series (49% at weaning and 38% at 30 days). The estimated total cost of treating 20 patients with VA-ECMO is $361,211 assuming each patient spends 3 days on ECMO. The estimated budget impact (additional costs incurred by the use of ECMO) of treating a patient with VA-ECMO for 3 days is $13,289.35.
- ECMO is a resource-intensive technology, and the recent rise in ECMO cases at the MUHC has placed an increased burden on limited resources, including perfusionist time. There is a need for dedicated funding to ease this burden and avoid unwanted delays in access to care.

Recommendations

- VA-ECMO for cardiogenic shock: Despite the absence of convincing evidence of superiority of VA-ECMO over alternative treatments for patients in cardiogenic shock, this technology has become widely accepted. We thus recommend an approval for evaluation of VA-ECMO in selected cardiogenic shock patients.
- ECPR for in-hospital cardiac arrest: In view of the limited evidence that ECPR may improve survival rates compared to CPR alone, as well as the wide acceptance of this technology, it is recommended that this intervention continue to be made available within the MUHC. We thus recommend an approval for evaluation of ECPR for in-hospital cardiac arrest patients.
- ECPR for out-of-hospital cardiac arrest: Currently, these cases are not treated with ECMO at the MUHC. Given the limited evidence that ECPR may improve

VA-ECMO in adult cardiac patients xvii June 26, 2017 Technology Assessment Unit, MUHC neurologically-intact survival in out-of-hospital cardiac arrest patients, and the availability of ECMO at the MUHC, we recommend an approval for evaluation of ECPR for out-of-hospital cardiac arrest patients, which is conditional on:

    - procurement of dedicated funding to ease the burden on resources associated with an increase in ECMO use;
    - establishment of an ECMO team.

- All of the above recommendations are conditional on:
    - systematic documentation of each case;
    - re-evaluation of the evidence as new data, or new technology, become available.
- The following recommendations apply to VA-ECMO (including ECPR) and VVECMO:
    - Any further increase in ECMO cases performed at the MUHC must be preceded by dedicated funding to sustain the increased use, including funding for outside referrals, and for perfusionists or nurses trained to replace perfusionists at the bedside. Such a dedicated budget is necessary to avoid unwanted delays in access to care due to a diversion of perfusionist services, and to reduce the burden on perfusionists.
    - Given that the decision to insert ECMO is made by cardiac surgeons and intensivists, the creation of a designated multi-disciplinary ECMO team comprising personnel from these specialties is necessary to foster efficient decision-making and faster deployment of ECMO, which may improve clinical outcomes.
    - We strongly recommend that the following variables be systematically documented for each case of ECMO: indications for use, reasons for choosing ECMO over alternative treatments, patient characteristics identified as relevant in the literature, time to deployment, complications, survival, and neurological outcomes.

  - A protocol should be developed outlining potential indications and contraindications, weaning criteria, and ethical considerations, to establish clear guidelines for the use of ECMO at the MUHC,
  - In order to promote optimal resource utilization, a quality review process for ECMO should be established. VA-ECMO in adult cardiac patients xviii June 26, 2017 Technology Assessment Unit, MUHC
  - The MUHC should register its adult ECMO site with ELSO, thus contributing valuable data to this vast, international registry.
- Given the limited evidence base and that ECMO is a rapidly evolving technology; this report should be updated as new information becomes available.

Plerixafor as first-line choice for stem cell mobilization in non-Hodgkin's lymphoma and multiple myeloma patients

Title

Plerixafor as first-line choice for stem cell mobilization in non-Hodgkin's lymphoma and multiple myeloma patients

Requestor

Celine Dupont, Department of Pharmacy

Publication Date

July 17, 2017

Authors

Nisha Almeida, Lama Saab, and Nandini Dendukuri

Background

Multiple myeloma and non-Hodgkin's lymphoma are hematopoietic cancers that are often treated with autologous hematopoietic stem cell transplants (aHSCT). Traditionally, regimens used to mobilize stem cells from the peripheral blood for aHSCT include growth factors such as G-CSF, with or without chemotherapeutic drugs like cyclophosphamide. Although cyclophosphamide is considered to be more effective than G-CSF in mobilizing stem cells, it is associated with greater complications rates, longer treatment duration, and greater unpredictability in scheduling apheresis sessions, placing a higher burden on resource use. Plerixafor is a novel agent that has high effectiveness in stem cell mobilization without the adverse effects of chemo-mobilization, and was approved by Health Canada in 2011 for use in conjunction with G-CSF as a stem cell mobilization agent in MM and NHL patients. The high cost of plerixafor has hindered its widespread adoption as first-line treatment, wherein all patients are administered plerixafor upfront. In an attempt to contain costs, several institutions have developed algorithms to add plerixafor to the standard regimen only in those patients with a demonstrated risk of failure to mobilize (poor mobilizers). In June 2015, the MUHC switched from a mobilization regimen of cyclophosphamide plus G-CSF to an upfront plerixafor regimen.

Conclusions

- Plerixafor is a novel mobilization agent that has considerable advantages over the alternatives. It is more effective than either G-CSF alone or cyclophosphamide plus G-CSF in mobilizing sufficient stem cells for transplantation, and it is not associated with the severe complications and unpredictability of cyclophosphamide mobilization.
- The main disadvantage of plerixafor is its high cost. Published studies and an evaluation of our local MUHC experience have found upfront plerixafor regimens to be more expensive than other mobilization regimens, mainly due to the high cost of the drug.
- In order to mitigate these high costs, some institutions have developed risk-adapted algorithms for the use of plerixafor only in those patients at risk of poor mobilization. Studies that evaluated such pre-emptive plerixafor regimens versus G-CSF only or cyclophosphamide plus G-CSF have reported good mobilization rates.
- Furthermore, our analysis of local data found that projected costs associated with pre-emptive plerixafor regimens using either G-CSF alone, or cyclophosphamide plus G-CSF, were considerably lower than that of an upfront plerixafor mobilization regimen, making the adoption of such regimens a more attractive option at the MUHC.

Recommendations

- Given the superiority of plerixafor over other regimens in mobilizing stem cells, we recommend:
    - Approval of a pre-emptive plerixafor regimen wherein all patients are mobilized with G-CSF, and only the subset of poor mobilizers receive plerixafor. This regimen is not associated with the severe complications and unpredictability of chemo-mobilization, but may result in higher costs due to more frequent use of plerixafor needed to salvage poor mobilizers.
    - Approval of a pre-emptive plerixafor regimen wherein all patients are mobilized with cyclophosphamide + G-CSF, and only the subset of poor mobilizers receive plerixafor. This regimen is associated with a greater risk of complications, but may result in lower costs

due to the higher mobilization rates of cyclophosphamide versus G-CSF alone.

    - Non-approval of routine use of upfront plerixafor as first-line treatment in NHL and MM patients undergoing autologous stem cell transplantation, due to the high costs associated with upfront plerixafor use. This recommendation may be re-evaluated in light of new evidence, or a drop in the drug price of plerixafor.

- We recommend that the Stem Cell Transplant Program develop a protocol for the choice of which pre-emptive plerixafor regimen is best suited to which patient.
- We recommend that the Stem Cell Transplant Program continue to systematically document treatment regimens, complications, and outcomes in patients mobilized from autologous stem cell transplants to allow for retrospective evaluation of the time to mobilization and the percentage of patients requiring plerixafor.
- We recommend that appropriate measures be undertaken to resolve discrepancies in the number of plerixafor vials dispensed by the department of Pharmacy and reported number used by the Stem Cell Transplant Program.
- Given that an ancillary benefit of upfront plerixafor use is a reduction in the wait list for stem cell collection, there is a need to evaluate the current infrastructure (number of apheresis beds, access to apheresis facilities) at the MUHC such that the non-use of upfront plerixafor does not hinder timely access to care for stem cell transplant patients.

KNOWLEDGE TRANSLATION ACTIVITIES

Collaborations

- Dr. Felipe Forero represented TAU at a meeting of hospital-based technology assessment units in Quebec organized at INESSS on 16th May 2017.
- TAU collaborated with INESSS on a field evaluation on the use of defibrillators across Quebec hospitals.

Teaching Activities

- Dr. Nandini Dendukuri and Dr. James Brophy taught a 2-credit course, EPIB 670: Introduction to Health Technology Assessment, during the summer at the Department of Epidemiology, Biostatistics and Occupational Health, McGill University.

Presentations

Oral

- Dr. Nisha Almeida presented "Stepping into the gap: The role of health technology assessment in translating evidence into policy that informs clinical decision-making" at the Centre for Outcomes Research Seminar at the MUHC on January 25, 2018.

- Dr. Nisha Almeida presented “Stepping into the gap: The role of health technology assessment in translating evidence into policy that informs clinical decision-making” at the Hopital du Scare-Coeur de Montreal Seminar on February 8, 2018.

Publications

Selected Peer-Reviewed Publications Related to Technology Assessment Activities:

- Almeida ND, Suarthana E, Dendukuri N, Brophy JM. Cardiac Resynchronization Therapy in Heart Failure: Do Evidence-Based Guidelines Follow the Evidence? Circulation: Cardiovascular Quality and Outcomes. 2017 Dec;10(12).
- Semret M, Schiller I, Jardin BA, Frenette C, Loo VG, Papenburg J, McNeil SA, Dendukuri N. Multiplex Respiratory Virus Testing for Antimicrobial Stewardship: A Prospective Assessment of Antimicrobial Use and Clinical Outcomes Among Hospitalized Adults. J Infect Dis. 2017 Nov 15;216(8):936-944.
- Xie X, Sinclair A, Dendukuri N. Evaluating the accuracy and economic value of a new test in the absence of a perfect reference test. Res Synth Methods. 2017 Sep;8(3):321-332.
- Xie X, Yec C., Mitsakakis N. The Impact of the Underlying Risk in Control Group and Effect Measures in Non-Inferiority Trials With Time-to-Event Data: A Simulation Study 2018;10(5):376-383.
- Xie X. Wang M, Ng V. & Sikich N. Some issues for the evaluation of noninferiority trials. J. Comp. Eff. Res. (2018) 7(9), 835–843

Work in Progress

HTA projects:

- Use of Alteplase to preventing catheter malfunction in hemodialysis (requested by André Bonnici, Department of Pharmacy)
- Statistical characterization of lung nodules on CT scan in patients with primary cancer in another location (requested by Benoit Gallix, Department of Radiology)
- Evaluating the feasibility of integrating Apolipoprotein B tests alongside traditional lipid panel tests across the McGill RUIS (requested by Drs. Andre Dascal and Alan Sniderman)
- Development of a tool to aid in the prioritization of clinically pertinent health interventions at the MUHC (requested by Dr. Carolyn Freeman, Chair of the Clinical Pertinence Committee)
- Hydrogel Spacer to reduce rectal toxicity in prostate cancer radiotherapy (requested by Tarek Hijal, Department of Radiation Oncology)

Working papers for submission to peer-reviewed journals:

Almeida ND, Mines L, Nicolau I, Sinclair A, Forero F, Brophy JM, Mayo N, Dendukuri N. A framework for aiding the translation of scientific evidence into policy: The experience of a hospital-based technology assessment unit.

POSTSCRIPT

"The TAU attempts to adjust the services we offer to conform to the resources available in a transparent, logical, fair, and consistent fashion. While some of our recommendations have not supported the acquisition of a technology, and have thus "saved money", others have supported new developments because they have identified the benefits, and found them to be sufficient to justify the increased expenditure. Our sincere thanks are due to the many members of the MUHC who have assisted with data collection, to those who have served as Consultants, and to the members of the Committee who have dedicated many hours to the consideration of these problems."

Maurice McGregor