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Technology Assessment Unit of the McGill University Health Centre (MUHC)

Update of TAU Reports #77 and #78: Cardiac Resynchronization Therapy in Heart Failure and Atrioventricular Heart Block

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Report prepared for the Technology Assessment Unit (TAU) of the McGill University Health Centre (MUHC)

by

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Approved by the TAU Policy Committee via an online poll

Mission Statement

The MUHC Health Technology Assessment Unit (TAU) advises hospital administrators and clinical teams in difficult resource allocation decisions. Using an approach based on independent, critical evaluations of the available scientific evidence and a transparent, fair decision-making process, novel and existing medical equipment, drugs and procedures used by healthcare professionals are prioritized on a continuous basis ensuring the best care for life with the best use of resources.

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Brief reports are prepared in response to urgent requests for information or to update previous reports with new evidence; in such cases an in-depth evaluation is either not possible or is unnecessary. Brief reports are reviewed by the Manager of TAU and the Chair of the Policy Committee, and only submitted for approval to the Policy Committee when recommendations are updated.

Declaration of Conflicts of Interest

Members of TAU's research staff and policy committee declare no conflicts of interest.

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REPORT REQUESTOR

This report was originally requested by Ann Lynch, Associate Director General, Clinical Operations, Adult Missions, McGill University Health Centre.

TYPES OF RECOMMENDATIONS ISSUED BY THE TAU COMMITTEE

Type of recommendation	Explanation
Approved	• Evidence for relevant decision criteria, including efficacy, safety, and cost, as well as context-specific factors such as feasibility, is sufficiently strong to justify a recommendation that the technology be accepted, used and funded through the institutional operating budget
Approved for evaluation	• There is a reasonable *probability* that relevant decision criteria, including efficacy, safety, and cost, as well as context-specific factors such as feasibility, are favorable but the evidence is not yet sufficiently strong to support a recommendation for permanent and routine approval. • The evidence is sufficiently strong to recommend a *temporary* approval in a restricted population for the purposes of evaluation, funded through the institutional operating budget.
Not approved	• There is insufficient evidence for the relevant decision criteria, including efficacy, safety, and cost; • The costs of any use of the technology (e.g. for research purposes) should not normally be covered by the institutional budget.

DISCLAIMER

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SUMMARY

BACKGROUND

CRT, also known as biventricular pacing (BVP), was developed to improve coordination of ventricular contraction in patients with symptomatic heart failure despite best medical management. We updated the recommendations issued for cardiac resynchronization therapy (CRT) in heart failure and atrioventricular (AV) heart block.

OBJECTIVES

The objectives of this report are to assess:

- any changes in guidelines for CRT in heart failure and AV heart block
- the cost and budget impact of CRT use at the MUHC
- local evidence on the use of CRT at the MUHC

METHODS

We carried out a search for relevant health technology assessment (HTA) reports and clinical guidelines for CRT in heart failure patients published between 2015 and 2021. We obtained information from Dr. Vidal Essebag and the Electrophysiology team on current use of CRT at the MUHC.

FINDINGS

Guideline changes:

Heart failure: New guidelines from the European Society of Cardiology (ESC) have updated recommendations for heart failure patients. These guidelines are very similar to the 2013 Canadian guidelines, except for a more conservative recommendation in the ESC guidelines for heart failure patients with left bundle branch block (LBBB) and QRS interval 130-149 msec: the Canadian guidelines continue to recommend CRT but the new ESC guidelines have downgraded the strength of their previous recommendation to 'should be considered'.

Atrial fibrillation: New guidelines from ESC have upgraded recommendations for patients with atrial fibrillation (AF). Patients with AF with an ejection fraction (EF) <35% and LBBB with QRS>130ms should be considered for CRT. Recommendations for CRT are stronger in patients with AF with planned AV nodal ablation regardless of QRS duration: for heart failure with reduced ejection fraction CRT is recommended; for

moderately reduced ejection fraction CRT should be considered; and for preserved ejection fraction CRT may be considered.

Atrioventricular (AV) heart block**:** New guidelines from ESC have also upgraded recommendations for patients with AV block and reduced ejection fraction: CRT rather than right ventricular pacing is indicated for such patients who have an indication for ventricular pacing and high degree AV block, regardless of the New York Heart Association class, to reduce morbidity. CRT is still not recommended for AV block patients with normal left ventricular ejection fraction.

MUHC experience:

At the MUHC, procedure times have decreased with greater experience over the years. Compared to the 2014/2015 fiscal period, the number of initial CRT-P (pacemaker) and CRT-D (defibrillator) implantations during 2018-2020 were relatively stable but decreased in the 2020/2021 fiscal year due to the COVID-19 pandemic.

The average total cost per initial implant substantially decreased compared to the 2014/2015 fiscal period: currently it costs $8,446 for CRT-P (a decrease of $2,627) and $13,766 for CRT-D (a decrease of $9,241).

TAU's previous evaluation recommended the systematic collection of patient selection criteria and outcomes. The MUHC electrophysiology team reported that they have been entering data on all patients waiting for and having received CRT in the Système de gestion de l'accès aux services (SGAS), Quebec's Ministry of Health database to facilitate timely access to specialized medical services. A more accessible local database, the CardioReport information system, has been acquired but installation for the electrophysiology lab of the MUHC was delayed by the hospital due to other COVID related priorities.

CONCLUSIONS

- New guidelines from ESC have (1) downgraded the strength of their previous recommendation for heart failure patients with LBBB and QRS interval 130-149 msec to 'should be considered' for CRT; (2) upgraded recommendations for atrial fibrillation patients with EF<35% and LBBB with QRS>130ms to 'should be considered' for CRT; (3) recommended CRT for patients with heart failure with reduced ejection fraction (HFrEF <40%) regardless of NYHA class who have an indication for ventricular pacing and high degree AV block. CRT is still not recommended for AV block patients with normal LVEF.

- At the MUHC, the procedure times have decreased with greater experience over the years. The number of implantations has remained relatively stable, with a decrease during the COVID-19 pandemic.
- The average total cost per initial implant substantially decreased compared to the 2014/2015 fiscal period: the cost is currently $8,446 for CRT-P (decreased $2,627) and $13,766 for CRT-D (decreased $9,241).
- The CardioReport information system has been acquired to prospectively collect patient data, but has not been installed yet in the electrophysiology lab. Administrative data have been reported to the provincial government.

UPDATED RECOMMENDATIONS

We breakdown our recommendations based on the clinical guidelines as follow:

- **For heart failure patients**:
  - CRT is Approved for:
    - NYHA class II- IV ambulatory with LVEF ≤ 35%, QRS ≥ 150 msec, and LBBB morphology
  - CRT is Approved for Evaluation for:
    - NYHA class II- IV ambulatory with:
      - LBBB **and** QRS duration 130-149 msec
      - non-LBBB **and** QRS duration ≥130 msec.
    - Treatment of heart failure patients in this category requires systematic data collection of patient selection criteria and outcomes.
  - CRT is Not Approved for:
    - NYHA class I, irrespective of QRS duration and morphology
    - QRS duration < 130 msec, irrespective of NHYA class and QRS morphology:

- **For atrial fibrillation patients**:
  - CRT is Approved for:
    - Patients with symptomatic atrial fibrillation with reduced ejection fraction (HFrEF) i.e. <40% regardless of QRS duration where atrioventricular junction ablation is planned.
  - CRT is Approved for Evaluation for:
    - Atrial fibrillation patients other than the above criteria.

        - Systematic data collection of patient selection criteria and outcomes is necessary for this category.

- **For AV block patients**:
    - CRT rather than RV pacing is Approved for:
        - Patients with heart failure with reduced ejection fraction (HFrEF <40%) regardless of NYHA class who have an indication for ventricular pacing and high degree AV block
    - CRT is Not Approved for:
        - AV block patients with normal or preserved LVEF (≥ 50%)

- Clinical data need to be systematically collected for all patients implanted with a CRT device who do not fall in the 'Approved' categories, across all populations i.e., heart failure, atrial fibrillation, and AV block patients.

- As part of TAU's mandate to evaluate the impact of new and existing health interventions, we will follow-up with the electrophysiology team once the CardioReport database becomes available to evaluate local data on patient selection criteria and downstream clinical outcomes.

SOMMAIRE

Contexte

La TRC, également connu sous le nom de stimulation biventriculaire (SBV), a été développé pour améliorer la coordination de la contraction ventriculaire chez les patients souffrant d'insuffisance cardiaque symptomatique, malgré une meilleure prise en charge médicale. Nous avons mis à jour les recommandations émises pour la thérapie de resynchronisation cardiaque (TRC) dans l'insuffisance cardiaque et le bloc atrio-ventriculaire (AV).

Objectifs

Les objectifs de ce rapport sont d'évaluer:

- tous les changements dans les lignes directrices pour la TRC dans l'insuffisance cardiaque et le bloc AV
- le coût et l'impact budgétaire de l'utilisation du TRC au CUSM
- les données probantes locales sur l'utilisation de la TRC au CUSM

Méthodes

Nous avons effectué une recherche de rapports d'évaluation des technologies de la santé (ETS) pertinents et de directives cliniques publiés entre 2015 et 2021 pour la TRC chez les patients souffrant d'insuffisances cardiaques. Nous avons obtenu des informations du Dr Vidal Essebag et de l'équipe d'électrophysiologie sur l'utilisation actuelle de la TRC au CUSM.

Résultats

Modifications des directives:

Insuffisance cardiaque : La Société Européenne de Cardiologie (ESC) a mis à jour leurs recommandations pour les patients souffrant d'insuffisance cardiaque dans des nouvelles directives. Ces lignes directrices sont très similaires aux lignes directrices canadiennes de 2013, à l'exception d'une recommandation plus conservatrice dans les lignes directrices de l'ESC pour les patients souffrant d'insuffisance cardiaque avec bloc de branche gauche (BBG) et intervalle QRS de 130 à 149 ms : les lignes directrices canadiennes continuent de recommander la TRC, mais les nouvelles directives de l'ESC ont réduit la force de leur recommandation précédente à "devrait être considérée".

Fibrillation auriculaire: Les nouvelles directives de l'ESC ont mis à jour les recommandations pour les patients atteints de fibrillation auriculaire (FA). Les patients atteints de FA avec une fraction d'éjection (FE) < 35% et BBG avec QRS > 130 ms doivent être envisagés pour une TRC. Les recommandations pour la TRC sont plus fortes chez les patients atteints de FA avec une ablation nodale AV planifiée, quelle que soit la durée du QRS: la TRC est recommandée pour l'insuffisance cardiaque avec une fraction d'éjection réduite; la TRC doit être envisagée pour une fraction d'éjection modérément réduite; et la TRC peut être envisagé pour la fraction d'éjection préservée.

Bloc atrio-ventriculaire (AV): Les nouvelles directives de l'ESC ont également mis à jour les recommandations pour les patients ayant un bloc AV et une fraction d'éjection réduite: la TRC plutôt que la stimulation ventriculaire droite est indiquée pour les patients qui ont une indication de stimulation ventriculaire et de bloc AV à haut degré, indépendamment de la classe de la New York Heart Association, pour réduire la morbidité. Le TRC n'est toujours pas recommandé pour les patients ayant un bloc AV avec une fraction d'éjection ventriculaire gauche normale.

Expérience au CUSM:

Au CUSM, les délais d'intervention ont diminué avec l'expérience acquise au fil des ans. Par rapport à l'année fiscale 2014/2015, le nombre d'implantations initiales de TRC-C (cardiostimulateur) et de TRC-D (défibrillateur) au cours de la période 2018-2020 a été relativement stable, mais a diminué au cours de l'année fiscale 2020/2021 en raison de la pandémie de COVID-19.

Le coût total moyen par implant initial a considérablement diminué par rapport à l'année fiscale 2014/2015: il coûte actuellement 8 446$ pour le TRC-C (une diminution de 2 627$) et 13 766$ pour le TRC-D (une diminution de 9 241$).

L'évaluation précédente de TAU recommandait la collecte systématique des critères de sélection et des événements des patients. L'équipe d'électrophysiologie du CUSM a indiqué qu'elle a saisi les données de tous les patients en attente ou ayant reçu une TRC dans le Système de gestion de l'accès aux services (SGAS), la base de données du Ministère de la Santé du Québec, afin de faciliter l'accès en temps opportun aux services médicaux spécialisés. Une base de données locale plus accessible, le système d'information CardioReport, a été acquise, mais l'installation dans le laboratoire d'électrophysiologie du CUSM a été retardée par l'hôpital en raison d'autres priorités liées à la COVID.

CONCLUSIONS

- Les nouvelles directives de l'ESC ont (1) réduit la force de leur recommandation précédente pour les patients souffrant d'insuffisance cardiaque avec un BBG et un intervalle QRS de 130-149 ms à 'devrait être envisagé' pour la TRC; (2) mis à jour les recommandations pour les patients atteints de fibrillation auriculaire avec une fraction d'éjection < 35% et BBG avec QRS >130 ms pour 'devraient être envisagées' pour la TRC; (3) recommandé la TRC pour les patients souffrant d'insuffisance cardiaque avec fraction d'éjection réduite (<40%), quelle que soit la classe NYHA, qui ont une indication pour la stimulation ventriculaire et un bloc AV à haut degré. La TRC n'est toujours pas recommandé pour les patients ayant un bloc AV avec une FEVG normale.

- Au CUSM, les délais d'intervention ont diminué avec l'expérience acquise au fil des ans. Le nombre d'implantations est resté relativement stable, mais a diminué pendant la pandémie de COVID-19.

- Le coût total moyen par implantation initiale a considérablement diminué par rapport à l'année fiscale 2014/2015: le coût est actuellement de 8 446$ pour le TRC-C (diminution de 2 627$) et de 13 766$ pour le TRC-D (diminution de 9 241$).

- Le système d'information CardioReport a été acquis pour recueillir prospectivement les données des patients, mais n'a pas encore été installé dans le laboratoire d'électrophysiologie. Les données administratives ont été communiquées au gouvernement provincial.

RECOMMANDATIONS

Nous avons séparé nos recommandations en fonction des directives cliniques comme suit:

- **Pour les patients atteints de l'insuffisance cardiaque**:
  - TRC est approuvée pour :
    - Classe II-IV ambulatoire NYHA avec FEVG ≤ 35%, QRS ≥ 150 msec et une morphologie BBG
  - TRC est approuvée pour évaluation pour :
    - Classe II-IV ambulatoire NYHA avec :
      - BBG et QRS d'une durée 130-149 msec
      - non-BBG et QRS d'une durée ≥130 msec.

    - Le traitement des patients souffrant d'insuffisance cardiaque dans cette catégorie nécessite une collecte systématique de données sur les critères de sélection et des évènements des patients.
  - TRC n'est pas approuvée pour:
    - Classe I NYHA, quelle que soit la durée du QRS et de la morphologie
    - Une durée QRS <130 msec, quelle que soit la classe NHYA et la morphologie QRS:

- **Pour les patients atteints de fibrillation auriculaire**:
  - TRC est approuvée pour:
    - Les patients présentant une fibrillation auriculaire symptomatique avec une fraction d'éjection réduite, c'est-à-dire < 40%, quelle que soit la durée du QRS, lorsqu'une ablation de la jonction auriculo-ventriculaire est prévue.
  - TRC est approuvée pour évaluation pour:
    - Les patients atteints de fibrillation auriculaire autres que les critères ci-dessus.
    - Une collecte systématique de données sur les critères de sélection et des évènements des patients est nécessaire pour cette catégorie.

- **Pour les patients avec bloc AV:**
  - TRC plutôt que la stimulation VD est approuvée pour:
    - Les patients souffrant d'insuffisance cardiaque avec une fraction d'éjection réduite (<40%), quelle que soit la classe NYHA, qui ont une indication de stimulation ventriculaire et de bloc AV à haut degré
  - TRC n'est pas approuvée pour:
    - Les patients ayant un bloc AV avec FEVG normale ou préservée (≥ 50%)

- Les données cliniques doivent être systématiquement collectées pour tous les patients implantés avec un appareil TRC qui ne relèvent pas des catégories 'Approuvé', dans toutes les populations, c'est-à-dire les patients souffrant d'insuffisance cardiaque, de fibrillation auriculaire et de bloc AV.

- Dans le cadre du mandat de TAU d'évaluer l'impact des interventions de santé nouvelles et existantes, nous ferons un suivi avec l'équipe d'électrophysiologie une fois que la base de données CardioReport sera disponible pour évaluer les données locales sur les critères de sélection des patients et les évènements cliniques en aval.

LIST OF ABBREVIATIONS

AF	Atrial fibrillation
AV	Atrioventricular
BVP	Biventricular pacemaker
CCS	Canadian Cardiovascular Society
CRT	Cardiac resynchronization therapy
CRT-P	CRT pacemaker
CRT-D	CRT with defibrillator
EF	Ejection fraction
ESC	European Society of Cardiology
HF	Heart failure
HFrEF	Heart failure with reduced ejection fraction
HR	Hazard ratio
HTA	Health Technology Assessment
ICD	Implantable cardioverter defibrillator
LBBB	Left bundle branch block
LVEF	Left ventricle ejection fraction
MUHC	McGill University Health Centre
NYHA	New York Heart Association
OPT	Optimal pharmacologic therapy
QALY	Quality adjusted life-year
QOL	Quality of life
QRS	The duration of the Q, R, and S waves on an electrocardiogram; a prolonged QRS duration (≥120 msec) on an electrocardiogram is considered to be a marker of ventricular dyssynchrony
RCT	Randomized controlled trial
RVP	Right ventricular pacing
SGAS	Système de gestion de l'accès aux services, Quebec's Ministry of Health database to facilitate timely access to specialized medical services
TAU	MUHC Technology Assessment Unit

UPDATE OF TAU REPORTS #77 AND #78: CARDIAC RESYNCHRONIZATION THERAPY IN HEART FAILURE AND ATRIOVENTRICULAR HEART BLOCK

1. BACKGROUND

Cardiac resynchronization therapy (CRT), also known as biventricular pacing, was developed to improve coordination of ventricular contraction in patients with symptomatic heart failure despite best medical management. CRT uses a biventricular pacemaker (BVP) to pace the right and left ventricles simultaneously, and is thus used to treat ventricular dyssynchrony, a difference in timing between right and left ventricular contractions. CRT, when implanted alone, is referred to as CRT-P (for pacing). For selected patients at risk of malignant ventricular arrhythmias, CRT can be combined with an implantable cardioverter defibrillator (ICD) and is then referred to as CRT-D (for defibrillator). Landmark trials show that cardiac resynchronisation therapy (CRT) is beneficial to selected heart failure patients as it can prolong life, reduce heart failure hospitalizations, and improve patient quality of life.

Heart block or AV block is a conduction disorder. It can range from asymptomatic first degree heart block to severe third degree block associated with a high risk of sudden cardiac arrest and death. Third degree block is an indication for right ventricular pacing (RVP). Nonetheless, RVP may induce left ventricular (LV) dysfunction and ventricular dyssynchrony which may contribute to heart failure (HF) over time. The use of BVP as an initial mode of pacing in AV block patients remains conflicting depending on the status of the left ventricular ejection fraction.

1.1 Reason for Brief Report

This brief statement is to update the recommendations issued in TAU report #77 (February 2016) and TAU report #78 (March 2016), which evaluated the effectiveness and safety of CRT in heart-failure (1) and in atrioventricular (AV) heart block (2), respectively.

At the time of the report evaluating CRT in heart failure, there was sufficient evidence to support the use of CRT for heart failure patients with New York Heart Association (NYHA) Class II/III, severely prolonged QRS interval (>150 msec); left bundle branch block (LBBB) morphology, and left ventricular ejection fraction (LVEF) <30%. The TAU Policy Committee therefore issued a recommendation of Approved for Evaluation, conditional

on careful consideration of patient clinical characteristics, such as QRS interval and LBBB morphology; and a systematic collection of patient data.

With respect to CRT in atrioventricular (AV) heart block (2), our review revealed that in AV block patients with normal left ventricular ejection fraction (LVEF), the use of CRT as an initial mode of pacing in AV block patients was unsupported because the evidence showed no significant difference in clinical endpoints compared to RVP. In AV block patients with low LVEF, there is fairly consistent evidence of modest improvement of ventricular function (increased LVEF, reduced end systolic volume, improved walk test), and modest symptomatic improvement (NYHA score and QoL). However, these improvements could be attributable to the fact that these studies often included a substantial number of patients with characteristics that are indications for CRT in heart failure. Moreover, there was no evidence of any effect of CRT on mortality or urgent care hospital visits. The TAU Policy Committee therefore issued a recommendation of Not Approved in AV block patients with normal LVEF and Approved for Evaluation in AV block patients with reduced LVEF.

Until April 2015, the device cost of a CRT-P with three leads was $8,470 compared to $3,768 for a dual-chamber pacemaker. The device cost of a CRT-D with three leads was $20,235 compared to $16,020 for a dual-chamber ICD. Given the increasing use, high costs and residual uncertainty regarding benefit of CRT in certain patients, TAU recommended the creation of a registry to assess local practice patterns and outcomes and further contribute to the overall evidence base.

2. OBJECTIVES

The objectives of this report are to assess:

- any changes in guidelines for CRT in heart failure and AV heart block
- the cost and budget impact of CRT use at the MUHC
- local evidence on the use of CRT at the MUHC

3. METHODS

3.1 Literature search and quality assessment

We carried out a search for relevant health technology assessment (HTA) reports and clinical guidelines for CRT in heart failure and AV block patients published between 2016 and 2021.

3.2 MUHC experience

We obtained information from Dr. Vidal Essebag and the Electrophysiology team on current use of CRT at the MUHC.

4. RESULTS

4.1 CRT in Heart Failure

The European Society of Cardiology (ESC) Guidelines published updated guidelines in 2016(3) and 2021(4), which modified indications for cardiac resynchronization therapy (CRT) in comparison with the 2012 ESC Guidelines(5). The main changes include (Table 1):

- No CRT for NYHA Class I irrespective of LBBB morphology and QRS interval;
- No CRT i.e. class III recommendation (contra-indication) in patients with a QRS duration <130 ms irrespective of LBBB morphology;
- CRT may be considered (class IIb) for patients with non-LBBB and QRS interval 130-149 msec
- Change from class I (CRT is recommended) to IIa (CRT should be considered) for all heart failure patients with LVEF ≤ 35%, LBBB and QRS interval 130-149 msec, regardless of their NYHA class.

The 2021 ESC guidelines are very similar to the 2013 Canadian Cardiovascular Society (CCS) guidelines(6), except for a more conservative recommendation in the ESC guidelines for heart failure patients with LBBB and QRS interval 130-149 msec: the Canadian guidelines continue to recommend CRT, but the new ESC guidelines have downgraded the strength of their previous recommendation to 'should be considered' (Table 1). QRS duration >150 msec remains the strongest predictor of CRT response.

The 2021 guidelines from ESC have upgraded recommendations for patients with Atrial Fibrillation (AF). Patients with AF with EF <35% and LBBB with QRS>130ms should be considered for CRT (Table 2). Recommendations for CRT are stronger in patients with AF with planned AV nodal ablation regardless of QRS duration: for heart failure with reduced ejection fraction, CRT is recommended; for moderately reduced ejection fraction, CRT should be considered; and for preserved ejection fraction, CRT may be considered.

4.2 CRT in Heart Block

In August 2016, the ESC released their guidelines with a recommendation for CRT rather than RV pacing for patients with heart failure with reduced ejection fraction (HFrEF <40%) regardless of NYHA class who have an indication for ventricular pacing and high degree AV block in order to reduce morbidity (3). This class I recommendation was an upgrade from class IIa recommendation in the 2013 ESC Guidelines (5) and remains in place in the 2021 ESC Guidelines (4).

CRT is still not recommended for AV block patients with normal LVEF.

5. CRT AT THE MUHC

5.1 Data on usage

Usage data for the 2018/2019 to 2020/2021 fiscal years at the MUHC show that dual chamber standard pacemakers remain the most implanted device (Figure 1). The use of standard pacemakers at the MUHC has been increasing over time. Compared to 2014/2015 fiscal period, initial CRT-P and CRT-D implantations during 2018-2020 were relatively stable but decreased in 2020/2021 fiscal year due to the COVID-19 pandemic.

In a personal communication, Dr. Vidal Essebag explained that the procedure times have decreased with greater experience over the years. Currently, the average procedure time at the MUHC is close to 90 minutes and often close to 60 minutes in some straightforward procedures. This is in line with a meta-analysis involving 29,503 CRT patients from 164 studies that demonstrated a declining trend in the mean rates of failure of implantation of an LV lead (>7.5% in 1998 to <2.5% in 2011). The failure rate declined from 5.4% (95% CI: 4.4% to 6.5%) in studies commencing before 2005 to 2.4% (95% CI: 1.9% to 3.1%; $p < 0.001$) in studies from 2005 onward (7).

Moreover, Dr. Essebag explained that implantation tools have improved for better efficacy and safety. “There are lots of new delivery systems that help get the lead to more ideal locations. For example, the use of quadripolar leads (i.e., four electrodes) showed better results than uni- or bipolar (one or two electrodes) that were used in the landmark trials. Improved pacing thresholds, novel pacing algorithms and longer battery life of newer devices will reduce/delay cost/morbidity related to replacements”. A study done in 847 patients showed that quadripolar leads had lower total mortality (adjusted hazard ratio [aHR]: 0.32, 95% CI 0.20-0.52), cardiac mortality (aHR: 0.36, 95% CI 0.20-

0.65), and heart failure hospitalization (aHR: 0.62, 95% CI 0.39-0.99) compared to non-quadripolar leads (8).

5.2 Data on patient characteristics

One of the conditions of the 2016 TAU report was that data on patient selection criteria and outcomes be systematically collected. Like other centers in Quebec that implant CRT, the MUHC electrophysiology (EP) must enter information on all patients waiting for and having received CRT in the Système de gestion de l'accès aux services (SGAS), Quebec's Ministry of Health database to facilitate timely access to specialized medical services. However, this administrative database is not easily accessible for quality improvement and evaluation purposes and does not contain all the variables of interest. Recently, a local database, the CardioReport information system (provider Medireport - Medical IT Solutions d.o.o.), has been acquired for both the Catheterization and EP labs at the MUHC. It was installed in the catheterization lab in January 2021, but the installation for the EP lab was delayed by the hospital due to other COVID-related priorities. It is possible to integrate forms into CardioReport to collect patient characteristics and outcomes to enable the evaluation of local evidence on the safety and efficacy of CRT. Table 3 lists patient selection criteria and outcomes to be documented for CRT patients treated at the MUHC.

5.3 Costs of CRT at the MUHC

In the 2019/2020 fiscal year, the MUHC spent $388,500 on 46 CRT-P implants (Figure 2). The cost was $8,446 per initial implant, which is $2,627 lower than the 2014/2015 fiscal period. In the same period, $1,046,200 was spent on 76 CRT-D implants. The cost was $13,766 per initial implant, which is $9,241 lower than the 2014/2015 fiscal period. The average price of the devices substantially decreased about 6 years ago with new pricing based on a multi-centre contract (with same prices for all implanting centres in Montréal). All CRTs costs including device and operational costs, with or without defibrillators (CRT-P or CRT-D), are fully funded by the Quebec government.

5.4 Treatment policy

According to Dr. Essebag, the 2013 Canadian Cardiology Society (6) and ECS guidelines (4) have been followed for patient indication. Patients who meet these indications are approved and funded by the government at all Quebec EP centres.

6. CONCLUSIONS

- New guidelines from ESC have (1) downgraded the strength of their previous recommendation for heart failure patients with LBBB and QRS interval 130-149 msec to 'should be considered' for CRT; (2) upgraded recommendations for atrial fibrillation patients with EF<35% and LBBB with QRS>130ms to 'should be considered' for CRT; (3) recommended CRT for patients with heart failure with reduced ejection fraction (HFrEF <40%) regardless of NYHA class who have an indication for ventricular pacing and high degree AV block. CRT is still not recommended for AV block patients with normal LVEF.

- At the MUHC, the procedure times have decreased with greater experience over the years. The number of implantations has remained relatively stable, with a decrease during the COVID-19 pandemic.

- The average total cost per initial implant substantially decreased compared to the 2014/2015 fiscal period: the cost is currently $8,446 for CRT-P (decreased $2,627) and $13,766 for CRT-D (decreased $9,241).

- The CardioReport information system has been acquired to prospectively collect patient data, but has not been installed yet in the electrophysiology lab. Administrative data have been reported to the provincial government.

7. RECOMMENDATIONS

We breakdown our recommendations based on the clinical guidelines as follow:

- **For heart failure patients**:
  - CRT is Approved for:
    - NYHA class II- IV ambulatory with LVEF ≤ 35%, QRS **≥** 150 msec, and LBBB morphology
  - CRT is Approved for Evaluation for:
    - NYHA class II- IV ambulatory with:
      - LBBB **and** QRS duration 130-149 msec
      - non-LBBB **and** QRS duration ≥130 msec.
    - Treatment of heart failure patients in this category requires systematic data collection of patient selection criteria and outcomes.
  - CRT is Not Approved for:
    - NYHA class I, irrespective of QRS duration and morphology

    - QRS duration < 130 msec, irrespective of NHYA class and QRS morphology:

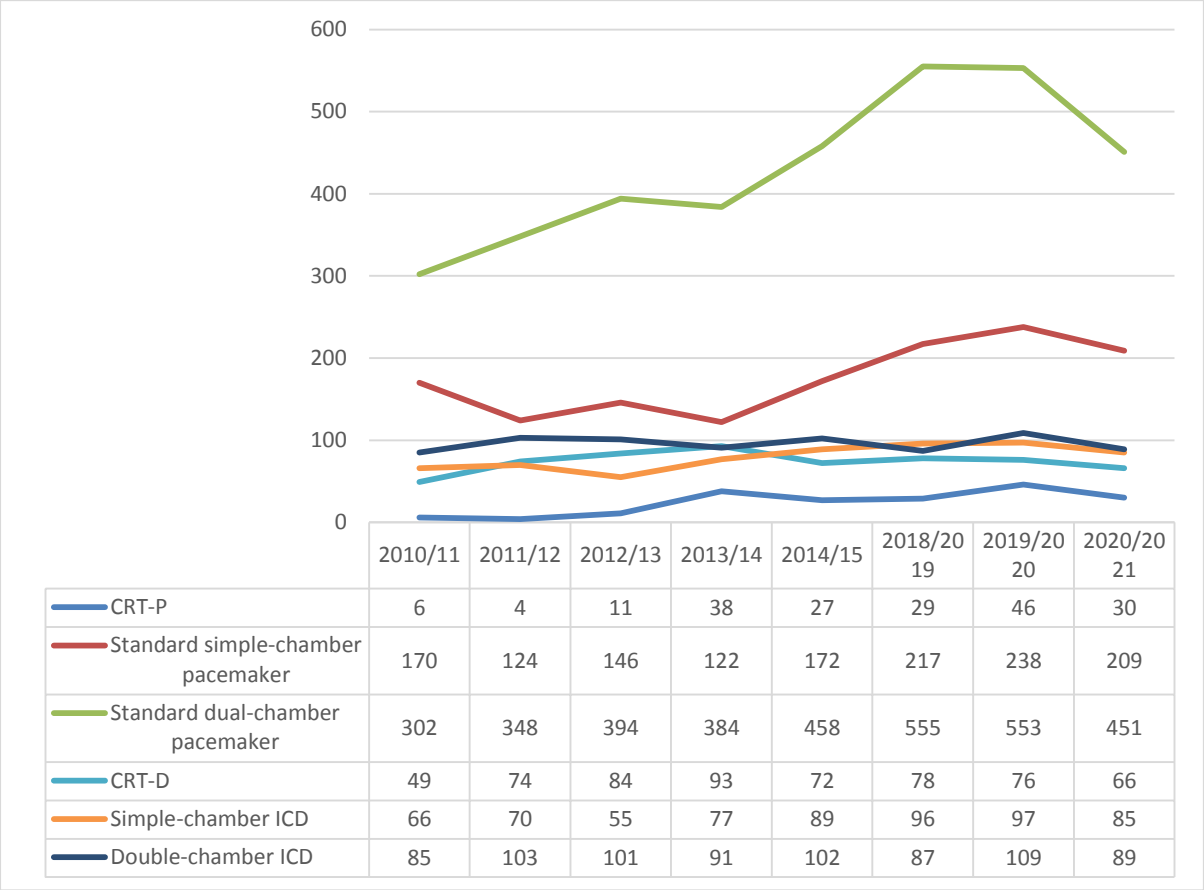
- **For atrial fibrillation patients**:
    - CRT is Approved for:
        - Patients with symptomatic atrial fibrillation with reduced ejection fraction (HFrEF) i.e. <40% regardless of QRS duration where atrioventricular junction ablation is planned.
    - CRT is Approved for Evaluation for:
        - Atrial fibrillation patients other than the above criteria.
        - Systematic data collection of patient selection criteria and outcomes is necessary for this category.

- **For AV block patients**:
    - CRT rather than RV pacing is Approved for:
        - Patients with heart failure with reduced ejection fraction (HFrEF <40%) regardless of NYHA class who have an indication for ventricular pacing and high degree AV block
    - CRT is Not Approved for:
        - AV block patients with normal or preserved LVEF (≥ 50%)

- Clinical data need to be systematically collected for all patients implanted with a CRT device who do not fall in the 'Approved' categories, across all populations i.e., heart failure, atrial fibrillation, and AV block patients.

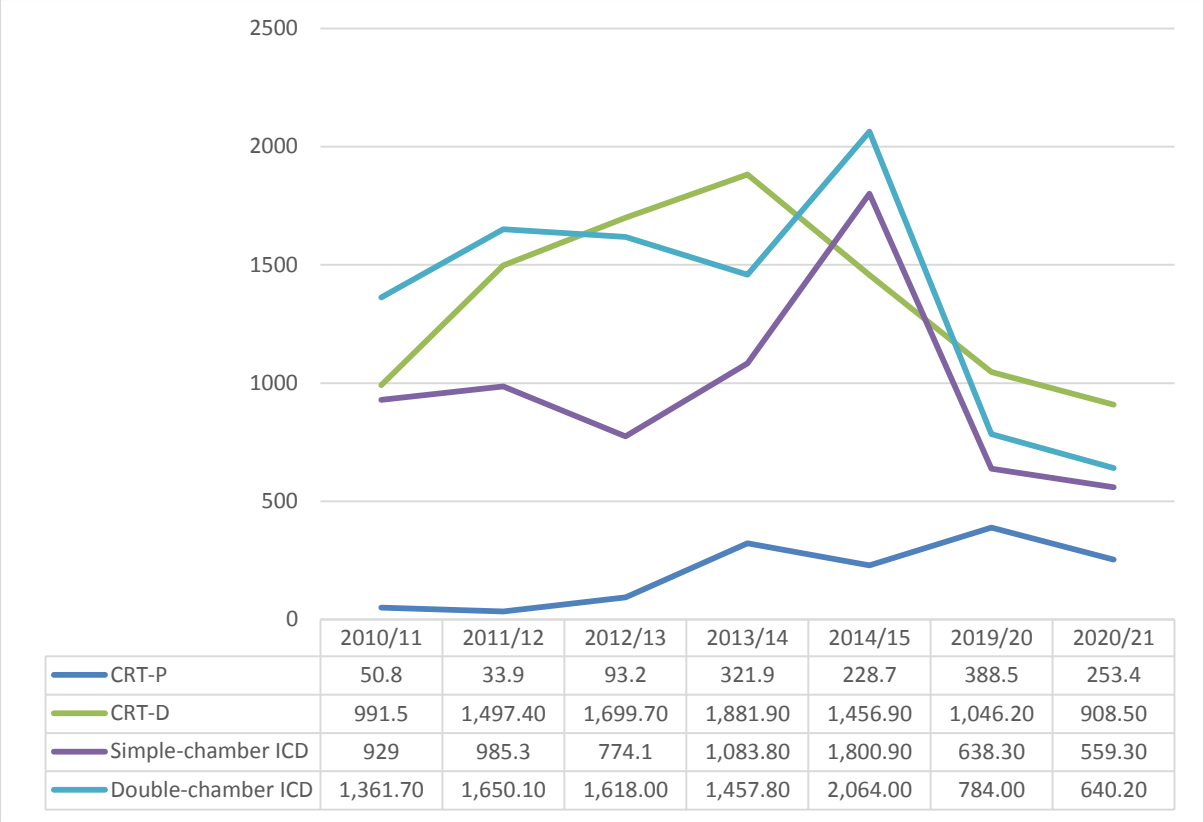
- As part of TAU's mandate to evaluate the impact of new and existing health interventions, we will follow-up with the electrophysiology team once the CardioReport database becomes available to evaluate local data on patient selection criteria and downstream clinical outcomes.

FIGURES



	2010/11	2011/12	2012/13	2013/14	2014/15	2018/2019	2019/2020	2020/2021
CRT-P	6	4	11	38	27	29	46	30
Standard simple-chamber pacemaker	170	124	146	122	172	217	238	209
Standard dual-chamber pacemaker	302	348	394	384	458	555	553	451
CRT-D	49	74	84	93	72	78	76	66
Simple-chamber ICD	66	70	55	77	89	96	97	85
Double-chamber ICD	85	103	101	91	102	87	109	89

Figure 1. Number of initial CRT implants at the MUHC



	2010/11	2011/12	2012/13	2013/14	2014/15	2019/20	2020/21
CRT-P	50.8	33.9	93.2	321.9	228.7	388.5	253.4
CRT-D	991.5	1,497.40	1,699.70	1,881.90	1,456.90	1,046.20	908.50
Simple-chamber ICD	929	985.3	774.1	1,083.80	1,800.90	638.30	559.30
Double-chamber ICD	1,361.70	1,650.10	1,618.00	1,457.80	2,064.00	784.00	640.20

Figure 2. Costs of initial CRT implants (in 1,000 CAD) at the MUHC

TABLES

Table 1. Summary of the clinical guidelines for the use of CRT in heart failure

Clinical Characteristics			Guidelines		
NYHA class	QRS morphology	QRS duration	Canadian Guidelines 2013	ESC 2012	ESC 2021
I	LBBB	120-129 msec	No CRT		No CRT
		130-149 msec	No CRT		No CRT
		≥ 150 msec	No CRT		No CRT
	Non-LBBB	120-129 msec	No CRT		No CRT
		130-149 msec	No CRT		No CRT
		≥ 150 msec	No CRT		No CRT
II	LBBB	120-129 msec	No CRT		No CRT
		130-149 msec	Recommend CRT	Recommend CRT-D	CRT should be considered
		≥ 150 msec	Recommend CRT	Recommend CRT-D	Recommend CRT-D
	Non-LBBB	120-129 msec	No CRT		No CRT
		130-149 msec	Unclear		CRT may be considered
		≥ 150 msec	CRT may be considered	Consider CRT-D	CRT should be considered
III	LBBB	120-129 msec	No CRT	Recommend CRT-D/P	No CRT
		130-149 msec	Recommend CRT	Recommend CRT-D/P	CRT should be considered
		≥ 150 msec	Recommend CRT	Recommend CRT-D/P	Recommend CRT-D/P
	Non-LBBB	120-129 msec	No CRT		No CRT
		130-149 msec	Unclear		CRT may be considered
		≥ 150 msec	CRT may be considered	Consider CRT-D/P	CRT should be considered

IV-ambulatory	**LBBB**	120-129 msec	No CRT	Recommend CRT-D/P	No CRT
		130-149 msec	Recommend CRT	Recommend CRT-D/P	CRT should be considered
		≥ 150 msec	Recommend CRT	Recommend CRT-D/P	Recommend CRT-D/P
	Non-LBBB	120-129 msec	No CRT		No CRT
		130-149 msec	Unclear		CRT may be considered
		≥ 150 msec	CRT may be considered	Consider CRT-D/P	CRT should be considered

Colour guide for class of recommendation

I	Recommended because benefit >>> risk
IIa	Considered because benefit >> risk
IIb	May be considered because benefit ≥ risk
III	Do not recommend
	Unclear
Blank	No recommendation

Table 2. Summary of the clinical guidelines for the use of CRT in atrial fibrillation

Clinical characteristics	Canadian Guidelines 2013	ESC 2012	ESC 2021
AF with permanent HF	CRT may be considered	CRT should be considered for NYHA class III and ambulatory IV, LVEF ≤ 35%, QRS ≥ 120, LBBB	CRT should be considered for NYHA class III and ambulatory IV, LVEF ≤ 35%, QRS **≥ 130**, LBBB
AF with planned AV nodal ablation regardless of QRS duration			CRT is recommended for heart failure with reduced ejection fraction
			CRT should be considered for heart failure with moderately reduced ejection fraction
			CRT may be considered for heart failure with preserved ejection fraction

AF = atrial fibrillation; AVJ = atrioventricular junction; CRT = cardiac resynchronization therapy; EF = ejection fraction; HF = heart failure; HFrEF = heart failure with reduced ejection fraction (≥50%) according to the 2021 ESC HF Guidelines; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; RV = right ventricular

Colour guide for class of recommendation

I	Recommended because benefit >>> risk
IIa	Considered because benefit >> risk
IIb	May be considered because benefit ≥ risk
III	Do not recommend
	Unclear
Blank	No recommendation

Table 3: Patient selection criteria and outcomes to be documented for CRT patients treated at the MUHC

Date:					**Hospital name:**
Patient ID:					
PATIENT CHARACTERISTICS					**COMMENTS**
Age (years)					
Sex	☐ Male				
	☐ Female				
NYHA class	☐ I				
	☐ II				
	☐ III				
	☐ IV	☐ ambulatory	☐ non-ambulatory		
Stress test or 6-min walk test performed?	☐ Yes	No. of METS completed:_____			
		Distance walked in 6 mins:_____			
	☐ No	Reasons:			
LBBB	☐ Yes				
	☐ No	☐ RBBB	☐ IVCD	☐ Other:	
AV block	☐ Yes				
	☐ No				
Ischemic etiology of heart failure	☐ Yes				
	☐ No				
QRS duration (msec)					
LVEF (%)					
Referring physician preference for specific device?	☐ Yes	Type of device:			
	☐ No	Name of referring institution:			
Patient preference for specific device?	☐ Yes	Type of device:			
	☐ No				
DEVICE CHARACTERISTICS					
Type of device	☐ CRT-P				
	☐ CRT-D	☐ Brava Quad	☐ Quadra Assura	☐ Viva Quad	
	☐ Pacemaker	☐ Single	☐ Dual	☐+ MRI	
	☐ ICD	☐ Single	☐ Dual	☐ +MRI	

Type of implant	☐ de novo			
	☐ re-implant	Date of previous implant:		
	☐ upgrade	Previous device:		
		Date of previous implant:		
OUTCOMES				**COMMENTS**
Adverse events associated with implantation procedure	☐ Implant failure			
	☐ Lead dislodgement			
	☐ Pocket hematoma			
	☐ Pneumothorax			
	☐ Other			
Heart failure hospitalizations since implant	☐ Yes	Number of hospitalizations:		
		Date of last hospitalization:		
	☐ No			
Mortality	☐ Alive			
	☐ Dead	☐ Cardiac death	☐ Non-cardiac death	
Quality of life measures	☐ MLWHF	Score:	Change since last visit:	
	☐ SF 36	Score:	Change since last visit:	
	☐ Patient self-report			

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