ABSTRACT

Background: In patients with acute coronary syndromes (ACS), guidelines recommend the assessment of left-ventricular ejection fraction (LVEF). Many patients with ACS undergo multiple assessments of LVEF, the clinical value of which is unknown.

Methods: Patients with ACS undergoing cardiac catheterization between 2012 and 2016 were evaluated and assessments of LV function identified. To evaluate changes in LVEF over time, available serial TTE assessments for a subsample of patients were examined.

Results: Of 8989 patients, 2723 (30.3%) had serial TTEs. Of these, 1515 (55.7%) had 2 or more assessments. In patients with ACS at index hospitalization, 30.6% had normal LV function, 18.7% had mildly reduced LV function, and 50.7% had moderately to severely reduced LV function. Of patients who had serial TTEs, 61.0% had normal LV function at index hospitalization, 29.1% had mildly reduced LV function, and 10.9% had moderately to severely reduced LV function. The mean LVEF for the entire cohort was 52.3% ± 12.7% at index hospitalization and 51.9% ± 13.3% at follow-up. At follow-up, 22.4% had mildly reduced LV function and 14.5% had moderately to severely reduced LV function.

Conclusion: The assessment of LVEF in patients with ACS is frequent, with multiple assessments occurring in the majority of patients with ACS presenting to this high-volume cardiac catheterization centre. This practice may influence the need for revascularization and device-based therapies.

RéSUMÉ

Contexte : En cas de syndrome coronarien aigu (SCA), les lignes directrices recommandent d’évaluer la fraction d’éjection ventriculaire gauche (FEVG). Beaucoup de patients présentant un SCA subissent plusieurs évaluations de la FEVG, une pratique dont on ne connaît pas la valeur clinique.

Méthodologie : Nous avons examiné les dossiers de patients atteints d’un SCA ayant subi un cathétérisme cardiaque entre 2012 et 2016.

Low-value care presents major health and economic burdens to the Canadian health care system.1,2 One avenue for quality improvement may involve the reduction of routine cardiac testing. Following acute coronary syndromes (ACS), the assessment of left-ventricular ejection fraction (LVEF) function is indicated to determine prognosis and guide therapy.3 Frequently, patients with ACS undergo multiple assessments of LV function in the patient journey. Guidelines do not specify the optimal number of LV assessments in patients with ACS. The American College of Cardiology/American Heart Association ST-Elevated Myocardial Infarction (ACC/AHA STEMI) guidelines4 support contrast left ventriculography at the time of cardiac catheterization and transthoracic echocardiography (TTE) on the second or third postadmission day for cases in which mechanical complications are suspected. In patients with moderate to severe LV dysfunction, a reassessment of LV function at least 40 days later is strongly recommended to guide the need for device-based therapy.5-7 The non–ST-elevation (NSTEMI) ACS guidelines8 similarly recommend assessment of LV function, but TTE is the preferred imaging modality.

For patients with ACS and preserved or mildly reduced LV function at the time of their events, the recommendations regarding postdischarge surveillance remain less clear. This has important implications as more than two-thirds of patients with NSTEMI and nearly one-half of patients with STEMI have relatively preserved LV function.9 In principle, a single assessment of LV function should be sufficient to direct guideline-based therapy in the majority of patients with ACS and preserved LV systolic function.10,11

The objective of our study was to assess the practice of LV assessment in patients with ACS presenting to a high-volume Canadian cardiac catheterization centre between 2012 and 2016. The results of the LV investigations performed at index hospitalization were evaluated. Furthermore, changes in LV function over time were examined in a subsample of patients who underwent serial assessments with TTE.

Methods

Patient cohort and data sources

There were 8989 patients who met the study inclusion criteria of presenting to the cardiac catheterization laboratory
Echocardiograms were reviewed in a subsample of patients with LVEF data available (n = 3221). Patients with ACS were classified into 3 groups: group 1 (LVEF > 50%), group 2 (LVEF 35% to 50%), and group 3 (LVEF < 35%).

Results: Our cohort consisted of 8327 patients with ACS (76% men), presenting with a mean age of 62.4 ± 12.4 years. At index presentation, 66% of patients had an LVEF > 50%, 27% had an LVEF between 35% and 50%, and 7% had severely reduced LVEF of < 35%. More than half of the cohort (n = 4600) had follow-up assessment of LV function, performed over an average of 2.71 ± 1.31 years. In the subsample of 3221 patients, only 1.1% of those in group 1, and 5.1% of those in group 2, deteriorated to an LVEF < 35%.

Conclusions: Patients with ACS often undergo multiple assessments of LV function. Those with initially preserved EF rarely demonstrate a decline in EF to < 35%. A reduction in low-value cardiac tests may be an important first step in improving the quality of care for patients with ACS.

Data analysis

Patient data sources were merged to generate individual follow-up records with associated LV assessment results from index presentation through clinical follow-up when applicable. Patients grouped according to LV assessment were compared using 1-way analysis of variance (ANOVA) or a χ² test, and data were presented in mean ± standard deviation or count (%), as appropriate. Changes in LVEF values were assessed by Wilcoxon signed ranks test for paired difference in repeated measure of LVEF percent between index presentation, first clinical follow-up, and last clinical follow-up. A multiple logistic regression model (Supplemental Appendix S1) was developed to identify predictors of repeated LV assessments. The calculation of the incidence of clinical outcomes is described separately (Supplemental Appendix S1). In brief, to facilitate comparison, we age and sex standardized the incident rates using the negative binomial models and estimation method. We then calculated risk ratios (with 95% confidence intervals [CIs]) for all of the outcomes for both groups of patients: namely, those with and without follow-up LV assessment. To determine if repeat testing had a favourable impact on reducing recurrent events after the index event, we excluded subjects with recurrent events within the first 6 months of the index ACS (n = 1057). The rationale for this was that it would be unlikely that repeat testing in the first 6 months postevent would change the outcome of these events. When we included all subjects in a sensitivity analysis for the impact of additional testing on adverse events, the results were unchanged (data not shown). Finally, a temporal sequence analysis was performed, as described in the Supplemental Appendix S1. Significance was set at P < 0.05. Statistical analysis was performed on SPSS V25 (IBM Corp, Armonk, NY), SAS Enterprise 7.1 (SAS Institute, Cary, NC) and MS Excel 2016 (Microsoft Corp, Redmond, WA).
Results

Cohort characteristics

Our study cohort consisted of 8327 patients (76% male), with mean age 62.4 ± 12.4 years (Table 1). Of 8327, 66% of patients had LVEF > 50% (group 1), 27% LVEF 35% to 50% (group 2), and only 7% presented with LVEF < 35% (group 3). An LVEF < 35% was associated with increased age, male gender, diabetes mellitus, and a diagnosis of STEMI.

Pattern of LV assessments at index hospitalization

Contrast left ventriculography alone was the most frequently used method of LV assessment in this cohort, with a rate of 49.2% (Fig. 2). Nearly one-half of patients with ACS (46.5%) underwent dual assessments of LV function (contrast left ventriculography and TTE). Patients with reduced LVEF were more frequently associated with dual assessments of LV function (58.6% and 57.2% for low and intermediate LVEF, respectively) compared with those with preserved LV systolic function (40.8% rate of dual assessments of LV function; P < 0.001). Of those with dual testing, 48% had the echocardiogram following the index catheterization and LV angiogram.

Pattern of LV assessments post-hospital discharge

At follow-up, 4600 patients (55%) underwent further assessment of LV function with an average of 1.9 ± 1.4 assessments per patient (total assessments n = 8888) and an average follow-up time of 2.7 ± 1.3 years. TTE was the most frequently used modality and was performed in 78.2% of patients. Nuclear imaging assessments were performed in 11.7% of patients, whereas contrast left ventriculography and cardiac magnetic resonance were less commonly used diagnostic tools at 8.5% and 1.6%, respectively. An inverse relationship was observed between degree of LV function at index...
and having a follow-up assessment, $P < 0.001$ (Fig. 3). In addition, multiple follow-up echocardiograms were more common in group 3 patients (51%) compared with group 1 (31%) or group 2 (36%) subjects ($P < 0.001$).

### Changes in LV function after follow-up testing

To evaluate the changes in LVEF in patients with ACS who underwent additional testing after discharge from hospital, the results of TTEs from a subsample of patients were analyzed. The average follow-up time for these patients (n = 3221) was 2.7 ± 1.3 years. Of the 3221 patients, 80% had an assessment within 12 months of cardiac catheterization, with 67% having an assessment less than 6 months after cardiac catheterization (Supplemental Table S2). The majority of these patients (2230 of 3221, 69.2%) had echo at index presentation. The primary clinical indication for the follow-up TTE was assessment of LV function and/or cardiac structure in 90% of patients.

LV function did not change significantly in group 1 patients when LVEF at index presentation (59% [55 to 64]) was compared with the first clinical follow-up (60% [56 to 64], $P = 0.78$). A similar trend was observed between first and last clinical follow-ups in group 1 patients ($P = 0.21$) (Table 2).

 Patients in group 2 demonstrated a significant improvement in LVEF at first clinical follow-up (50% [43 to 58]) compared with index presentation (44% [39 to 47], $P < 0.001$). No significant changes in LVEF were noted in group 2 patients when the first (47% [40 to 56]) and last (48% [40 to 56]) clinical follow-ups were compared ($P = 0.168$).

Group 3 patients also demonstrated a significant improvement in LVEF when index presentation (29% [24 to 32]) was compared with the first clinical follow-up (37% [30 to 48], $P < 0.001$). A similar trend of improvement was observed in group 3 patients undergoing multiple assessments of LVEF ($P < 0.001$).

Of the 1848 patients with preserved LVEF at index presentation (group 1), 1641 (88.8%) remained in the same group at the first clinical follow-up, whereas 186 (10.1%) declined to group 2, and only 21 (1.1%) declined to group 3. The trends for the other groups at index presentation are summarized in Table 3. Similar trends are also seen between first and last follow-up LV function assessment (Supplemental Table S3). In subjects with a quantitative LVEF value in follow-up (n = 1848), 7.2% dropped from an EF of > 40% to an EF of < 40%. This further confirms the general finding that LVEF does not decrease significantly in the vast majority of individuals with relatively preserved EF at baseline.

### Predictors of repeated LV assessment in ACS patients

Reduced index LVEF, history of dyslipidemia, STEMI and NSTEMI presentation, female sex, and history of revascularization were significantly associated with additional LV assessments after hospital discharge (Table 4). Patients with severely reduced LV function were twice as likely to undergo further assessment of LV function compared with patients with normal LV function ($P < 0.001$; odds ratio [OR], 2.04; 95% CI, 1.70-2.45).

### Clinical outcomes

Patients with ACS who did not undergo follow-up assessment of LV function had no difference in the risk of mortality compared with those patients with ACS who underwent additional assessments of LV function (risk ratio [RR], 1.03 [95% CI, 0.78-1.37]; Table 5). Patients with MI (RR, 1.69; 95% CI, 1.36-2.10) unstable angina (RR, 2.82; 95% CI, 2.06 to 3.86), and heart failure presentations (RR, 1.72; 95% CI, 1.31-2.27) were more likely to have had an additional assessment of LV function. The timing of the event could not be determined. For these events, it is most likely that the repeat event led to further testing and not the converse.

### Discussion

In a cohort of contemporarily-managed patients with ACS presenting to the catheterization laboratory, the current study...
demonstrates the following: (1) The majority of patients have preserved LV function at index presentation; (2) almost one-half undergo dual assessments of LV function at index presentation; (3) more than 50% have additional assessments of LV function postdischarge; (5) nearly 90% of patients with ACS and initially preserved LV function at index presentation remain in a category of normal function on first clinical follow-up, with only 1.1% declining to an LVEF of <35%; and, importantly, (5) reassessments of LV function do not appear to be associated with improved outcomes.

Prognostic value of LV assessment

LV function is a powerful and independent prognosticator of clinical outcomes.9,12-14 For example, in 1 study evaluating LV function in patients with STEMI,13 1-year major adverse cardiovascular events were significantly increased in patients with LVEF <40% compared with those without LV systolic dysfunction. Of note, only 14% of patients in that cohort had evidence of LV dysfunction at clinical follow-up.

We hypothesized that a single assessment of LV function at index hospitalization would be sufficient in most patients. The findings from the current analysis are consistent with this. The majority of patients with ACS and preserved baseline LV function who underwent further reassessment did not demonstrate significant deterioration. Strikingly, in patients with both mild to moderately reduced, as well as severely reduced LV systolic function, significant improvements were observed at first clinical follow up, underscoring the importance of contemporary management in ACS patients with regard to recovery of LV function.
Our findings revealed only a very small proportion of patients with ACS and deteriorations in LV function to < 35% post-hospital discharge. Although limited compliance to aggressive secondary prevention or recurrent ischemia may represent only 2 of many important contributing factors, additional data are required to better understand which patients with ACS are likely to undergo these adverse changes.

Selective ordering of follow-up LV assessments

Routine serial assessments of LV function in patients ACS may represent low-value care, and this has been observed in other investigations. A recent study by Hua et al.15 found that repeat LV assessment in acutely admitted subjects leads to new findings in only 11% of patients. Another investigation, which evaluated hospitals that performed the highest rates of echocardiography in patients with acute MI, found an association with increased costs and slightly longer lengths of stay but no difference in clinical outcomes compared with hospitals that perform lower rates of echocardiography.16 In a large Canadian study evaluating noninvasive cardiac testing in patients with ACS,17 it was found that the rates of testing 1 year post-ACS are increasing with time and that the associated costs appear to be escalating out of proportion to the growth of ACS.

LV reassessment and outcome

Dual assessment of LV function using both contrast left ventriculography and TTE during index hospitalization occurred in 46.5%, including 40.8% of patients with preserved LV systolic function. Although there may be indications for additional testing at index presentation, such as valvular heart disease, reduction of testing at index presentation may result in both cost savings and reduction in contrast media delivered. The tests were performed approximately one-half of the time with echocardiography occurring after the catheterization and LV angiogram.

There was no difference in the incidence of mortality in patients with ACS who did not undergo a follow-up LV assessment in comparison with those who did. In addition, undergoing a left ventriculography or an echocardiography at baseline did not alter the perceived need for a follow-up echocardiogram, as the clinical outcomes between both groups were similar. There was higher morbidity in those with additional testing. However, we were unable to determine the sequence but believe that it was most likely the adverse event that was responsible for increased testing. These important findings strengthen the feasibility of a selective strategy of LV reassessment in patients with ACS and may ultimately have important implications in terms of enhancing the quality and value of cardiac care.

Study strengths and limitations

The strengths of this study include a large and representative cohort from the PCI era. Granular details regarding change in LVEF from index presentation to clinical follow-up were available in more than 3200 patients with ACS.

Nonetheless, as a single-centre retrospective cohort analysis, this investigation is subject to selection bias. Second, we did not have complete data on indications for repeat imaging in patients who underwent clinical follow-up (ie, present in only 1278 of 3221). However, for those in whom the indication was available, 90% of the follow-up assessments appeared to be performed to evaluate LV function. Third, we did not have data on completeness of revascularization; medication prescribing and adherence; and device therapies, which may affect both LVEF and outcomes. Fourth, we did not assess the impact of patient location of residence (rural vs urban) and follow-up with a specialist, which may influence

Table 2. Change in LVEF% by index LVEF groups

| Repeated measure | Index LVEF group 1 | Index LVEF group 2 | Index LVEF group 3 |
|------------------|-------------------|-------------------|-------------------|
|                  | Median (IQR)      | P                 | Median (IQR)      | P                 | Median (IQR)      | P                 |
| Index LVEF% vs First FU LVEF% | 59 (55-64) | 0.782             | 59 (55-64) | 0.001             | 59 (55-64) | 0.001             |
|                  | 60 (56-64)        | 50 (45-58)        | 37 (30-48)       | N = 745           | N = 211           |
| First FU LVEF% vs last LVEF%  | 59 (54-65) | 0.207             | 47 (40-56) | 0.168             | 41 (34-53)       | N = 93 |
|                  | N = 218           | 48 (40-56)        | N = 211           | N = 93           |

$P$ value assessed by Wilcoxon signed ranks test for paired difference.

FU, follow-up; IQR, interquartile range; LVEF, left-ventricular ejection fraction.

Table 3. Changes in LVEF groups

| Index LVEF group | First follow-up LVEF group | N (%) |
|------------------|-----------------------------|-------|
|                  | 1. LVEF > 50%               |       |
| 1. LVEF > 50% n = 1848 | 1641 (88.8)                 |       |
| 2. LVEF = 35-50% n = 1052 | 573 (54.5)                  |       |
| 3. LVEF < 35% n = 321  | 78 (24.3)                   |       |
| Patients with follow-up LVEF values | N = 3221 |       |
|                  | 2. LVEF = 35%-50%           |       |
|                  | 186 (10.1)                  |       |
|                  | 425 (40.4)                  |       |
|                  | 116 (36.1)                  |       |
|                  | 2292 (71.2)                 |       |
|                  | 727 (22.6)                  |       |
|                  | 202 (6.3)                   |       |

Data presented in count (%).

LVEF, left-ventricular ejection fraction.
Revascularization 1.322 1.002 1.744 0.048
NSTEMI 1.517 1.248 1.843
STEMI 1.783 1.463 2.173
Current smoking 0.933 0.839 1.036 0.195
Dyslipidemia 1.148 1.047 1.259 0.003
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STEMI 1.783 1.463 2.173 0.001
NSTEMI 1.517 1.248 1.843 0.001
Revascularization 1.322 1.002 1.744 0.048

\[ P\] value assessed by multiple logistic regression model. \( N = 8327; \) Nagelkerke \( R^2 = 0.028; \) Hosmer and Lemeshow test, \( P = 0.357. \)
CI, confidence interval; LVEF, left-ventricular ejection fraction; NSTEMI, non–ST-elevation myocardial infarction; Revascularization, history of percutaneous coronary intervention or coronary artery bypass grafting; STEMI, ST-elevation myocardial infarction.

both the ease-of-access and ordering patterns of LV assessment. Finally, a local quality-improvement initiative led by Chew and colleagues, which recommended repeat LV assessment in patients with ACS and EFs of < 45%, partially overlapped with the current analysis and may have resulted in a slightly increased number of TTEs ordered in this patient population.

**Clinical implications**

We estimate, conservatively, that at least one-third of the assessments of LV function were of low value in this cohort. In subjects with initially preserved LVEF, a single assessment of LV function at presentation, without the need for routine outpatient follow-up imaging, would be sufficient in the majority of cases. Very few such patients had significant decrease in LVEF during the index admission or in follow-up. This group represented two-thirds of our cohort. Almost one-half had repeat in-hospital assessments of LV function, and more than 50% had repeated outpatient assessments of LV function. Strategies to identify best-care pathways to avoid redundant testing would be particularly useful in this group. A selective approach to repeat testing based on clinical evolution could be considered for those with mild-to-moderate reduction in LVEF at presentation. Individual facilities should implement a knowledge translation approach that best works in their domain to determine if similar patterns exist locally and how change might occur. Finally, we need to implement strategies to ensure that the smaller group of those with severe reduction in LV function at presentation do have repeat LV function assessment at appropriate intervals to guide therapeutic decision making. Up to one-third of patients with EFs < 35% at index event did not have follow-up assessment. This is also a missed opportunity in this small group of patients and is the ongoing work of quality improvement projects.

**Conclusions**

The results from the current evaluation indicate that the majority of patients with ACS not only have preserved LV systolic function at index presentation but also frequently undergo multiple assessments of LV function during index presentation, as well as at clinical follow-up. Patients with preserved LV function rarely have declines in LV function to < 35%. This might provide an opportunity to reduce routine testing postevent.

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The authors have no conflicts of interest to disclose.

**Table 4. Predictors of follow-up LVEF assessments**

| Parameter                          | Odds ratio | 95% CI for odds ratio | Lower | Upper | \( P \) value |
|-----------------------------------|------------|-----------------------|-------|-------|---------------|
| Index LVEF (group 2 vs group 1)   | 1.502      | 1.356                 | 1.664 | < 0.001 |
| Index LVEF (group 3 vs group 1)   | 2.041      | 1.697                 | 2.455 | < 0.001 |
| Sex (male vs female)              | 0.882      | 0.794                 | 0.980 | 0.019 |
| Age                               | 0.997      | 0.993                 | 1.001 | 0.102 |
| Dyslipidemia                      | 1.148      | 1.047                 | 1.259 | 0.003 |
| Current smoking                   | 0.933      | 0.839                 | 1.036 | 0.195 |
| STEMI                             | 1.783      | 1.463                 | 2.173 | < 0.001 |
| NSTEMI                            | 1.517      | 1.248                 | 1.843 | < 0.001 |
| Revascularization                 | 1.322      | 1.002                 | 1.744 | 0.048 |

ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; CI, confidence interval; FU, follow-up; MI, myocardial infarction.

* Remove the patients (\( n = 1057 \)) having any events of the clinical outcomes within 6 months from the date of catheterization.

**Table 5. Risk of clinical outcomes for patients with ACS and follow-up LV assessments compared with patients having no follow-up LV assessments**

| Incident type | Group (n) | Number of patients for the incidence (%) | Person-years | Crude incidence rate per 100 person-years | Age- and sex-standardized incidence rate per 100 person-years | Risk ratio (95% CI) |
|---------------|-----------|-----------------------------------------|--------------|-------------------------------------------|-------------------------------------------------------------|----------------------|
| Death         | FU (3543)* | 232 (6.6)                               | 15,597.4     | 1.49                                      | 1.31 (0.96-1.78)                                             | 1.03 (0.78-1.37)     |
|               | No FU (3727)| 226 (6.1)                               | 15,229.5     | 1.48                                      | 1.27 (0.92-1.73)                                             |                      |
| MI            | FU (3543)* | 219 (6.2)                               | 18,963.3     | 1.15                                      | 1.22 (1.00-1.48)                                             | 1.69 (1.36-2.10)     |
|               | No FU (3727)| 133 (3.6)                               | 19,171.4     | 0.69                                      | 0.72 (0.58-0.90)                                             |                      |
| Unstable angina | FU (3543)* | 147 (4.2)                               | 19,094.9     | 0.77                                      | 0.74 (0.56-0.96)                                             | 2.82 (2.06-3.86)     |
|               | No FU (3727)| 53 (1.4)                                | 19,437.7     | 0.27                                      | 0.26 (0.19-0.37)                                             |                      |
| Heart failure | FU (3543)* | 129 (3.6)                               | 19,236.1     | 0.67                                      | 0.66 (0.48-0.91)                                             | 1.72 (1.31-2.27)     |
|               | No FU (3727)| 83 (2.2)                                | 19,342.7     | 0.43                                      | 0.38 (0.27-0.55)                                             |                      |
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Supplementary Material

To access the supplementary material accompanying this article, visit CJC Open at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2020.12.028.