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ORIGINAL RESEARCH

Pattern and Prognostic Impact of Regional Wall Motion Abnormalities in 255 697 Men and 236 641 Women Investigated with Echocardiography

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BACKGROUND: Regional wall motion abnormalities (WMAs) after myocardial infarction are associated with adverse remodeling and increased mortality in the short to medium term. Their long-term prognostic impact is less well understood.

METHODS AND RESULTS: Via the National Echo Database of Australia (2000–2019), we identified normal wall motion versus WMA for each left ventricular wall among 492 338 individuals aged 61.9±17.9 years. The wall motion score index was also calculated. We then examined actual 1- and 5-year mortality, plus adjusted risk of long-term mortality according to WMA status. Overall, 39 346/255 697 men (15.4%) and 17 834/236 641 women (7.5%) had a WMA. The likelihood of a WMA was associated with increasing age and greater systolic/diastolic dysfunction. A defect in the inferior versus anterior wall was the most and least common WMA in men (8.0% and 2.5%) and women (3.3% and 1.1%), respectively. Any WMA increased 5-year mortality from 17.5% to 29.7% in men and from 14.9% to 30.8% in women. Known myocardial infarction (hazard ratio [HR], 0.86 [95% CI, 0.80–0.93]) or revascularization (HR, 0.87 [95% CI, 0.82–0.92]) was independently associated with a better prognosis, whereas men (1.22-fold increase) and those with greater systolic/diastolic dysfunction had a worse prognosis. Among those with any WMA, apical (HR, 1.08 [95% CI, 1.02–1.13]) or inferior (HR, 1.09 [95% CI, 1.04–1.15]) akinesis, dyskinesis or aneurysm, or a wall motion score index >3.0 conveyed the worst prognosis.

CONCLUSIONS: In a large real-world clinical cohort, twice as many men as women have a WMA, with inferior WMA the most common. Any WMA confers a poor prognosis, especially inferoapical akinesis/dyskinesis/aneurysm.

Key Words: cohort ■ mortality ■ wall motion abnormality

Despite transformative ways in which individuals presenting with an acute coronary syndrome (ACS; including acute non-ST-segment–elevated and ST-segment–elevated myocardial infarction [MI]) are now managed with an early revascularization approach to preserve their myocardium and reduce the risk of mortality, coronary artery disease remains a leading cause of death worldwide.[1,2] The goal of ACS management is to prevent or minimize myocardial necrosis, with the echocardiographic manifestation being a left ventricular regional wall motion abnormality (WMA) event.[3,4] Post MI there are 3 important characteristics determine the likelihood of subsequent adverse remodeling.[5,6] First is the region of infarction of left ventricle (LV) muscle with the main regions being anterior, septal (including anteroseptal and inferoseptal regions), inferior, and lateral (inferolateral and anterolateral),[7] with each region corresponding to specific

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CLINICAL PERSPECTIVE

What Is New?

- In a very large unselected multicenter clinical cohort, we demonstrated that twice as many men as women were reported as having regional wall motion abnormalities (WMAs) during echocardiography.
- Inferior WMA (8.0% men, 3.3% women) was the most common, with hypokinesis more common than akinesis, dyskinesis, or aneurysm.
- Compared with normal wall motion, any WMA increased 5-year mortality from 17.5% to 29.7% in men and from 14.9% to 30.8% in women; inferior WMAs were associated with the worst prognosis, particularly in the presence of akinesis also affecting the apical wall.

What Are the Clinical Implications?

- Following a myocardial infarction, an individual's prognosis depends (at least partially) on the location and severity of any WMA, with akinesis, dyskinesis, and aneurysm associated with the worst prognosis.
- Tailored management decisions for each individual could include the prognostic impact of the presence, location, and severity of WMAs identified from echocardiography.

Nonstandard Abbreviations and Acronyms

NEDA	National Echo Database Australia
WMA	wall motion abnormality

coronary arterial blood supply. Second is the extent of involvement (ie, the number of myocardial segments involved) identified on echocardiography by the number of adjacent impaired myocardial segments.[7] Third is the percentage of LV wall that is replaced by fibrosis (scar thickness, indicating transmural infarction),[8,9] which is identified on echocardiography by akinesis (failure to contract) or dyskinesis (paradoxical outward motion during systole) usually accompanied by wall thinning once myocardial scarring is evident.[10] These regional WMA (RWMA) are readily identified by echocardiography.[11] If persistent post MI, they represent important risk factors for adverse remodeling,[12] especially in the presence of hypertension.[13–16] Thus, in contrast to those who recover normal myocardial function post ACS, individuals with persistent WMA may develop *adverse remodeling*, a complex pathophysiology that promotes development of heart failure, impaired quality of life, recurrent hospitalizations, and premature death.[17] Such individuals are the target of therapeutic agents such as angiotensin receptor-neprilysin inhibitors, aldosterone receptor antagonists,[18] SGLT-2 (sodium-glucose co-transporter type 2) antagonists,[19] and beta blocker therapies[20,21] that aim to reverse the neurohormonal cascade that drives adverse ventricular remodeling.[22] Some of the fundamental clinical issues arising from the current to future impact of these new treatment strategies are (1) what is the overall pattern of WMA seen in the general cardiac population (including those who present with silent pathology), and (2) how do they influence an individual's prognostic outlook? Surprisingly, there are few contemporary reports addressing these key issues.

Study Aims

We examined data from the National Echo Database of Australia (NEDA) cohort to describe (1) the underlying prevalence, distribution, and characteristics of RWMA) in adults being investigated with echocardiography (last recorded) on an age- and sex-specific basis, across the spectrum of LV function, and (2) the associated pattern of short- to long-term mortality associated with specific WMAs.

METHODS

The anonymized data and materials that support the finding of this study may be available from the corresponding author upon reasonable request.

Study Design and Setting

NEDA is a large observational registry that retrospectively and prospectively captures routinely acquired echocardiographic data from individuals typically referred by a primary care physician or cardiologist to investigate or follow-up cardiac disease Australia-wide. Data linkage to the National Death Registry[23] then permits survival analyses for each individual within this clinical cohort.[24] The census date for survival status was May 21, 2019. Listed causes of death were categorized according to *International Classification of Diseases, Tenth Revision, Australian Modification* (*ICD-10AM*) coding with the primary cause of death in the range of I00 to I99 categorized as cardiovascular related. All analyses and reporting conforms to the Reporting of Studies Conducted Using Observational Routinely-Collected Health Data Statement.[25] Informed consent was not necessary for this observational study of deidentified aggregated data. Ethical approvals for NEDA have been obtained from the University of Notre Dame Australia and all other relevant human research ethics committees and the study is registered with the Australian New Zealand Clinical Trials Registry (ACTRN12617001387314).

Study Data

The second iteration of the NEDA captured data from 23 centers Australia-wide. As described in greater detail previously,[24,26] a standardized protocol ensures that all echocardiography reporting data from participating centers are cleaned and transformed into a standard NEDA format. This process generates uniform echocardiographic profiling data, while removing duplicates and impossible measurements.[26]

An additional feature of NEDA is the capture of the echocardiographic report text, written by the echocardiographer/cardiologist as the final interpretation of the echocardiography study. For this study we applied an artificial intelligence-based, natural language processing program to scrutinize each report. A detailed description of natural language processing can be found in Data S1 and Figure S1. The natural language processing architecture was developed by Echo IQ Ltd to create an inference library to evaluate preprocessed bulk data in JSON format for anchor words followed by extraction of location and severity data in proximity to the anchor words. Configuration files (containing specific comment types, dictionaries, and qualitative and quantitative grading), python code (to correct misspellings, abbreviations, special characters, and valve identifiers), and helper functions (for conversion metrics) were all customized for this project. The natural language processing underwent multiple iterations using expert subspecialist echocardiography review of the outputs (D.P.) and was successfully trained to identify the following: (1) Presence of coronary artery disease (CAD) and an ACS (including MI and unstable angina); (2) revascularization procedure, including percutaneous angioplasty (with/without stenting) and coronary artery bypass grafting; (3) concurrent symptoms, including dyspnea and angina; (4) normal wall motion (NWM); (5) presence of any WMA; and (6) global left ventricular systolic dysfunction. For the presence of any WMA we captured data on the specific type (wall thinning, hypokinesis, akinesis, and aneurysm) and location (regional/segments [anterior, lateral, apical, septal, and inferior] versus global dysfunction) of each WMA documented. We used the standard American Heart Association[27] and American Society of Echocardiography[11] recommended nomenclature for myocardial segmentation using the 17-segment model for left ventricular regions. For the purposes of this study, the WMA region was simplified as follows:

- Anterior: any basal, mid, or apical anterior WMA.
- Lateral: anterolateral and inferolateral WMA in the basal or mid regions or the lateral apex.
- Inferior: any basal, mid, or apical inferior WMA.
- Septal: anteroseptal and/or inferoseptal WMA in the basal or mid regions or the septal apex.
- Apical: the apical cap (segment 17). If any of the other 4 apical regions were involved (anterior, lateral, inferior, or septal), they were included under the WMA for that wall.

Severity of each WMA was classified as hypokinesis (with search terms including mild hypokinesis and severe hypokinesis), akinesis, dyskinesis, or aneurysmal. Where more than 1 severity classification was provided in the same WMA region, the more severe was chosen (for example, akinesis of the basal inferior wall and hypokinesis of the mid-inferior wall was classified as inferior akinesis). In addition to extraction of reported global LV dysfunction from text comments, impaired LV ejection fraction (LVEF) was defined as a measured value of <60% for women and <55% for men.

Finally, the Wall Motion Score Index (WMSi) was calculated based on the location and severity of wall motion abnormalities recorded (3 anterior and inferior wall segments, 5 lateral and septal wall segments, and a single segment for the apex). Motion was numerically coded (normal = 1, hypokinesis = 2, akinesis = 3, dyskinesis or aneurysm = 4) and any abnormality was translated to all segments within that wall to create a total wall motion score for each region, and the WMSi was calculated for each WMA as the proportion of the total of 17 segments (with NWM = 1.0). Global abnormalities were not included as WMA.

Study Participants

Of 618 065 individuals investigated with echocardiography at 23 clinical sites, we excluded 16 762 cases investigated pre-2000 (a priori cutoff point), 3980 cases with lone dyssynchrony (due to pacing or the presence of a left bundle-branch block pattern of ventricular activation), and a further 118 744 (19.2%) in whom no mention of wall motion status (including no statement that wall motion was normal) were identified (Figure 1). Cases with global left ventricular systolic dysfunction (with the accompanying reduction in left ventricular systolic function) and global impairment of systolic function with regional variation (ie, the presence of a specific WMA in addition to global impairment affecting all other walls) were included. Based on their last recorded echocardiogram, the study cohort therefore comprised 492 338 individuals aged 61.9±17.9 years in whom (1) the presence/absence of a RWMA was reliably established and (2) there was individual data linkage to mortality.

Study Outcomes

Consistent with the study aims, our primary focus was describing the reported distribution and prevalence of specific WMAs across each region of the left ventricular myocardium at last reported echocardiogram, on

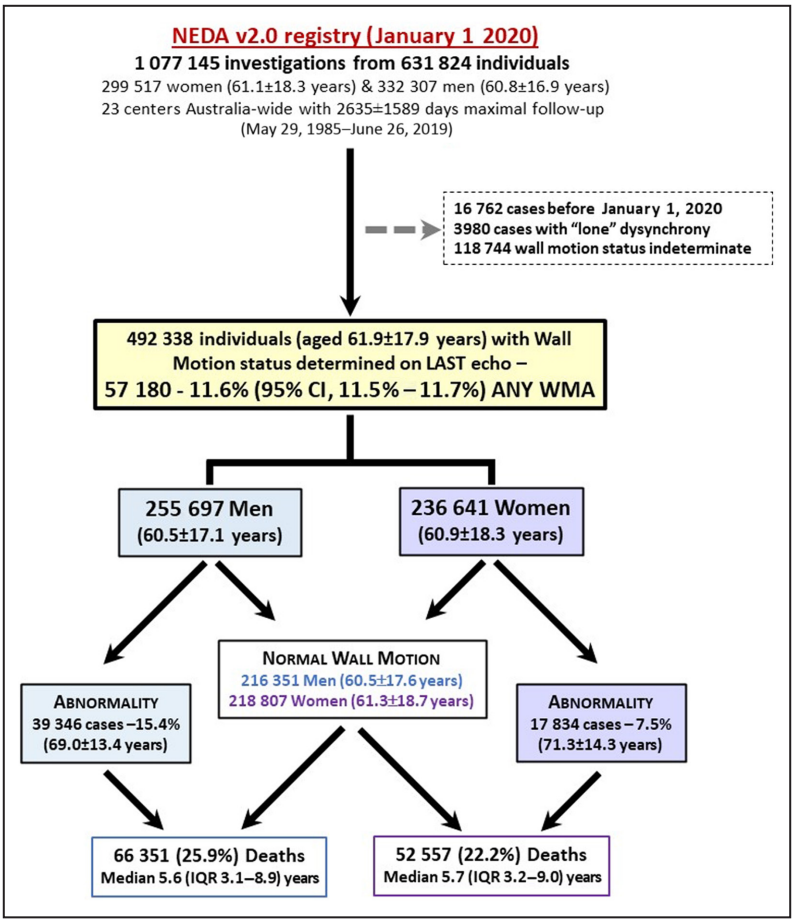

Figure 1. Study schema.
The study schema shows the number of potentially eligible cases who formed the study cohort once key exclusion criteria were applied, according to their wall motion status determined on last echocardiogram. IQR indicates interquartile range; NEDA, National Echocardiographic Database of Australia; and WMA, wall motion abnormality.

a sex-specific basis. We then examined the pattern of actual 1- and 5-year mortality and longer-term mortality (study census date May 2019) according to the pattern of RWMA during median 5.6 (interquartile range [IQR] 3.1–8.9) and 5.7 (IQR 3.2–9.0) years follow-up of men and women, respectively.

Statistical Analysis

Standard methods for reporting descriptive data included mean±SD, median (IQR), and proportions (%). Key independent variables for analysis were selected a priori and include sex (men or women), age (years), and presence of WMA at last echocardiogram. Between-group differences were examined per sex for all cohort characteristics according to wall motion status using Student *t* tests (or the nonparametric equivalent).

The pattern of WMA (any and according to region/specific type) is reported on a sex-specific basis, along with the proportion of cases who died from any cause at 1 and 5 years with full follow-up for those specific time points. The Kaplan–Meier method followed by Cox-proportional hazard models (entry method with proportional hazards confirmed by visual inspection) were used to derive adjusted hazard ratios (HRs) and 95% CI for the risk of mortality for all-cause deaths. All-cause mortality was examined by sex (men versus women) for all patients identified with a WMA reported on their last echocardiogram. Adjustments were made for age (yearly increments), body mass index (unit increments), repeated echocardiogram within the past 28 days, cohort year (in 5-year epochs), acute MI (AMI), any form of revascularization, LVEF, E wave velocity cm/s, tricuspid regurgitation velocity (all 3 parameters as per unit increments), and the specific WMA documented in each of the 5 regions. Given the potential confounding of age, we ran sensitivity analyses (applying the same models) for those above (median [IQR], 76 [70–81] years) and below (median 51 [IQR 39–59] years) the age of 65 years (at echocardiogram). All

statistical analyses were performed using SPSS version 28.0 software (SPSS Inc., Chicago, IL) with significance accepted at $P<0.05$.

RESULTS

Cohort Characteristics

The study cohort comprised 255 697 men (51.9%) and 236 641 women aged 60.5±17.1 and 60.9±18.3 years, respectively (see Figure 1). Of these, 84.6% of men (216 351 cases aged 60.5±17.6 years) and 92.5% of women (218 807 cases aged 60.9±18.3 years) had NWM reported on their last echocardiogram. Overall, therefore, 57 180 cases (11.6% [95% CI, 11.5%–11.7%]) had any form of WMA reported, with more than double the number of men versus women (15.4% versus 7.5%).

As summarized by Table 1, both men (39 346 cases aged 69.0±13.4 years) and women (17 834 cases aged 71.3±14.3 years) with WMA were much older ($P<0.001$ for both comparisons) than those with NWM. As expected, those with any form of WMA were far more likely to have a documented history of CAD or AMI and undergo a revascularization procedure ($P<0.001$ for all comparisons). They also demonstrated higher levels of LV systolic and diastolic dysfunction as demonstrated by significantly lower LVEF and stroke volume and higher E:E' and left atrial volume index levels ($P<0.001$ for all comparisons). Those with any RWMA also had higher pulmonary artery pressures, as evidenced by significantly higher ($P<0.001$) peak tricuspid regurgitation velocity. In keeping with improved revascularization after ACS over the past 2 decades, a progressively smaller proportion of men had WMA was observed since 2000 (13.5%, 9.6%, 7.0%, and 6.8% for each 5-year epoch), although the corresponding fall in women was less marked (6.4%, 4.4%, 3.1%, and 3.1%, respectively). The pattern of WMA remained similar over the 4 epochs.

Pattern of Wall Motion Abnormalities

Figure 2A summarizes the specific pattern of WMAs reported in 39 346 men. Overall, 2.8% had global dysfunction reported (LVEF 47.6±14.9%), with a distribution of global impairment similar across each WMA. The most affected region was the inferior wall (8.0%), and the least affected was the anterior wall (2.5%). In all 5 regions, hypokinesis followed by akinesis/dyskinesis combined were the most common forms of abnormality detected/reported, corresponding to a mean overall calculated WMSi of 1.57±0.58. Similarly, Figure 2B summarizes the specific pattern of WMAs reported in 17 834 women. Overall, 1.2% were reported to have global dysfunction (LVEF 50.2±15.1%). Like men, the most affected region was the inferior wall (3.3%), and the least affected was the anterior wall (1.1%). In all 5 regions, hypokinesis followed by akinesis/dyskinesis combined were the most common forms of abnormality detected/reported, with a mean overall calculated WMSi of 1.48±0.53.

Mortality According to Specific WMA

As shown in Figure 3, in both men (top panel A) and women (bottom panel B), actual 1- and 5-year all-cause mortality was relatively low in the presence of NWM (corresponding to a calculated WMSi=1.0), ranging from 4.3% to 5.6% at 1 year to 14.9% to 17.5% at 5 years. If any WMA was reported, these figures rose from 9.8% to 29.7% in men and 10.9% to 30.8% in women. Among those aged <65 years (model included 109 781 cases) any WMA was associated with an adjusted HR of 1.22 (95% CI, 1.13–1.31; $P<0.001$) for longer-term mortality, compared with 1.14 (95% CI, 1.11–1.18; $P<0.001$) for those aged ≥65 years (model included 82 180 cases). Overall, the combination of akinesis/dyskinesis/aneurysm was associated with higher mortality (at both time points) rates compared with hypokinesis. Among men, akinesis/dyskinesis/aneurysm in the inferior (34.7%) or lateral (36.4%) walls was associated with the highest 5-year mortality rates overall, with a markedly lower rate associated with anterior wall (28.9%), noting an average age differential of ~2.5 years among those with an inferior (older) versus anterior (younger) abnormality. This was reflected in all-cause mortality according to calculated WMSi—rising from 38.5% with a score of >1.0 to 1.49 (reference group) to 49.5% with a score ≥3.0 (age-adjusted HR, 1.27 [95% CI, 1.17–1.37]; $P<0.001$). In women, mortality rates were also highest in those akinesis/dyskinesis/aneurysm but with a more consistent pattern across all regions. As in men, this was reflected in all-cause mortality according to calculated WMSi, rising from 39.6% with a score of >1.0 to 1.49 (reference group) to 58.8% with a score ≥3.0 (age-adjusted HR, 1.38 [95% CI, 1.22–1.57]; $P<0.001$). In both sexes, global dysfunction was associated with a high rate of actual mortality at 1 and 5 years, with 42.2% of men (3061/7254) and 47.6% of women (1275/2678) dying during complete follow-up.

Figure 4 shows the fully adjusted risk of (long-term) all-cause mortality within the cohort men and women who had any form of WMA at their last echocardiogram. Overall, the risk of mortality was ~1.2-fold higher in men. Beyond the specific type of WMA, those cases who had an echocardiogram recorded in the 28 days before their last echocardiogram (indicating an acute change in their clinical status) were ~1.2-fold more likely to die, as were those with evidence of progressively worse diastolic and higher pulmonary

Table. Cohort Characteristics According to Wall Motion Status

	Men (N=255 697)		Women (N=236 641)	
	Normal (n=216 351)	WMA (n=39 346)	Normal (n=218 807)	WMA (n=17 834)
Demographic profile				
Age, y, mean±SD	60.5±17.6	69.0±13.4	61.3±18.6	71.3±14.3
Anthropometrics				
Body mass index, kg/m^2 (n=346 975)	28.2±5.7	28.0±5.2	28.1±7.1	27.5±6.5
Timing of echocardiography, n (%)				
2000–2004 (n=26 457)	10 456 (39.5%)	3561 (13.5%)	10 755 (40.7%)	1685 (6.4%)
2005–2009 (n=130 839)	56 277 (43.0%)	12 522 (9.6%)	59 319 (43.0%)	5721 (4.4%)
2010–2014 (n=208 412)	93 578 (44.9%)	14 686 (7.0%)	93 632 (44.9%)	6516 (3.1%)
2015–2019 (n=126 630)	56 040 (44.3%)	8577 (6.8%)	58 101 (45.9%)	3912 (3.1%)
Prior echocardiographic investigations				
Clinical history				
Prior coronary artery disease, n (%)	38 682 (17.9%)	19 942 (50.7%)	23 346 (10.7%)	6780 (38.0%)
Acute myocardial infarction, n (%)	16 347 (7.6%)	11 021 (28.0%)	9505 (4.3%)	4263 (23.9%)
Breathlessness, n (%)	17 707 (8.2%)	3964 (10.1%)	27 195 (12.4%)	2418 (13.6%)
Coronary artery bypass graft, n (%)	12 403 (5.7%)	7243 (18.4%)	3955 (1.8%)	1584 (8.9%)
Percutaneous transluminal coronary angioplasty, n (%)	7755 (3.6%)	4270 (10.9%)	4117 (1.9%)	1309 (7.3%)
Any revascularization, n (%)	19 369 (9.0%)	10 925 (27.8%)	7840 (3.6%)	2746 (15.4%)
Pulmonary artery pressures				
eRVSP, mm Hg (n=278 855)	32.5±10.7	36.2±11.5	32.5±11.1	37.0±12.1
TR peak velocity, m/s (n=278 855)	2.58±4.74	2.75±4.92	2.58±1.11	3.70±1.21
Left heart dimensions and function				
Left atrial volume index, mL/m^2 (n=182 642)	40.9±27.5	55.5±36.4	39.3±26.1	53.0±37.0
LV diastolic diameter, cm (n=397 273)	4.91±0.67	5.23±0.78	4.47±0.59	4.73±0.74
LV systolic diameter, cm (n=358 490)	3.17±0.74	3.77±0.95	2.78±0.58	3.29±0.86
LVEF, % (n=465 205)	61.1±12.2	50.8±15.1	65.0±10.4	53.8±15.3
Impaired LVEF, n (%)	49 924 (21.7%)	19 565 (49.7%)	59 202 (27.1%)	9778 (54.8%)
Mitral *E′* velocity, cm/s (n=234 979)	8.25±2.86	6.64±2.21	8.44±3.12	6.51±2.38
Mitral *E* wave velocity, cm/s (n=399 322)	78.2±25.7	79.1±27.8	84.0±27.0	85.9±30.7
Mitral *E*:*E′* ratio (n=211 194)	10.1±4.75	12.6±5.72	10.6±5.10	14.0±6.80
Stroke volume index, mL/m^2 (n=135 708)	41.3±12.3	37.5±11.3	40.1±11.9	35.9±11.1
Peak aortic velocity, m/s (n=381 633)	15.7±6.45	15.9±6.9	15.8±5.84	16.1±6.79
Follow-up/outcome				
Days from last echocardiogram/death	1821±1318	1576±1352	1903±1333	1562±1363
All-cause mortality, n (%)	50 403 (23.3%)	15 948 (40.5%)	44 958 (20.5%)	7619 (42.7%)
Cardiovascular-related mortality*, n (%)	14 226 (6.6%)	6380 (16.2%)	13 590 (6.2%)	3187 (17.9%)

eRVSP indicates estimated right ventricular systolic pressure; LV, left ventricular; LVEF, left ventricular ejection fraction; TR, tricuspid regurgitation; and WMA, wall motion abnormality. All values are presented as mean±SD unless otherwise stated. All-cause mortality is derived from the Australian National Death Index.

*Cardiovascular-related mortality is categorized according to *International Classification of Diseases, Tenth Revision, Australian Modification (ICD-10AM)* coding with the primary cause of death in the range of I00–I99 categorized as cardiovascular related.

pressure. Independent of those with progressively better LV systolic function (indicated by increasingly more preserved LVEF levels) and survival, those individuals with a documented history of AMI and a revascularization procedure also had a more favorable prognosis (as did those investigated in later years). Independent of all these factors, those with evidence of apical or inferior dyskinesis/ akinesis/aneurysm were more likely to die in the longer term. This contrasted with a decreased probability of death associated with the same abnormality recorded in the septal and anterior walls (once again noting that men, but not women, with an anterior abnormality were slightly younger on average). In a sensitivity analysis of those aged <65 years (109 781 in the full model) versus those aged ≥65 years (82 180 in the full model), these

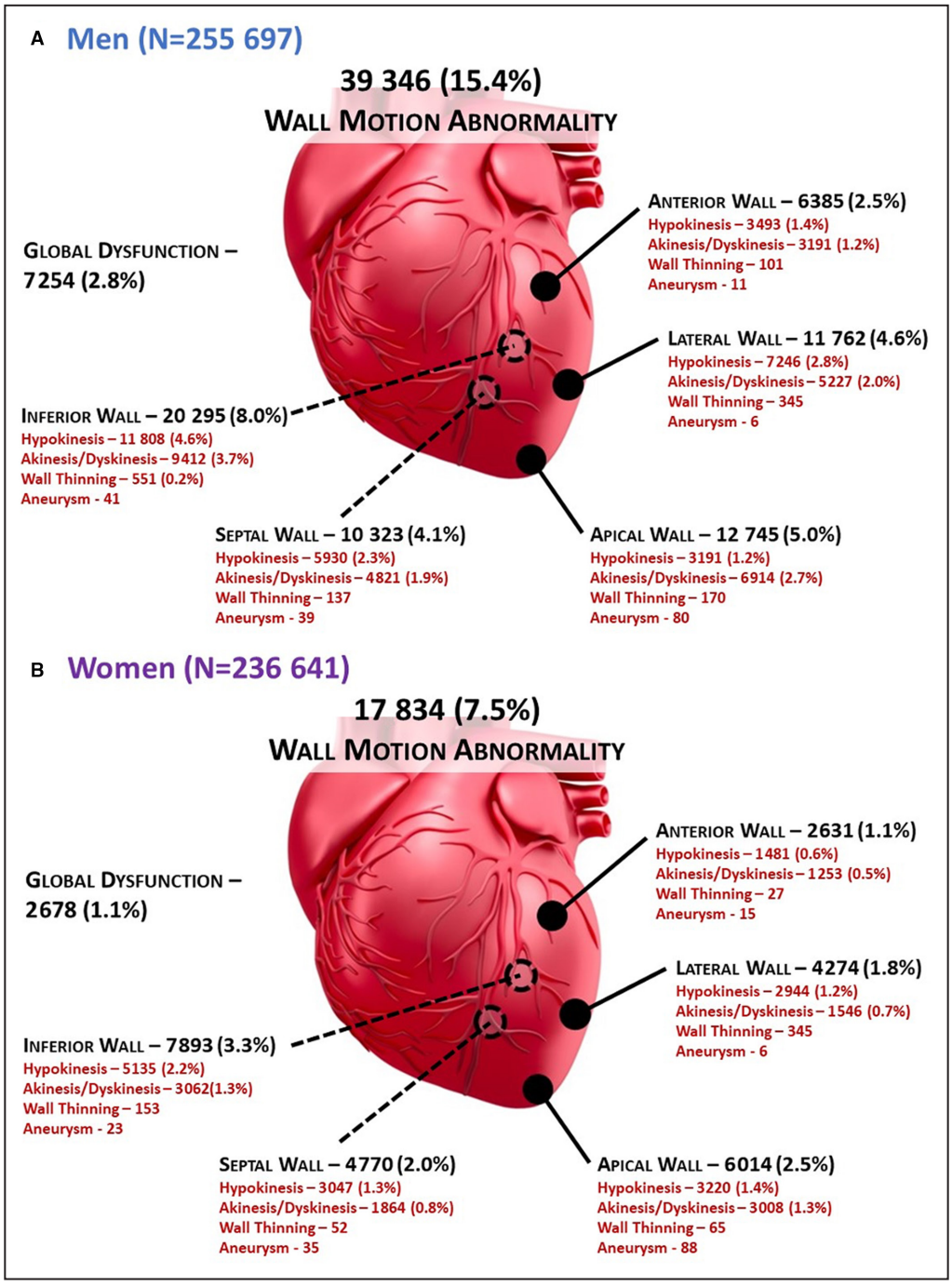

Figure 2. Specific pattern of wall motion abnormality (WMA) in 255697 men (A) and 236641 women (B).

This figure shows the proportion n (%) of WMA per wall (inferior, septal, apical, lateral, or anterior) for all men (n=255697) (**A**) and all women (n=236641) (**B**). **A**, A total of 39346 men had at least 1 WMA at last echocardiogram. Of these, 14828 (37.7%), 11360 (28.9%), and 13158 (33.4%) had 1, 2, and 3 or more regions with a reported WMA. Mean±SD age of those with global dysfunction was 67.8±13.1 years compared with 68.4±12.7, 67.6±13.4, 66.6±13.7, 68.2±12.9, and 65.8±13.7 years for those with an inferior, septal, apical, lateral, or anterior wall abnormality, respectively. **B**, A total of 17834 women had at least 1 WMA at last echocardiogram. Of these, 7433 (41.7%), 4680 (26.2%), and 5721 (32.1%) had 1, 2, and 3 or more regions with a reported WMA. Mean±SD age of those with global dysfunction was 71.6±13.7 years compared with 70.9±13.7, 70.0±14.3, 70.2±14.2, 71.3±13.4, and 70.0±14.2 years for those with an inferior, septal, apical, lateral, or anterior wall abnormality, respectively. WMA indicates wall motion abnormality.

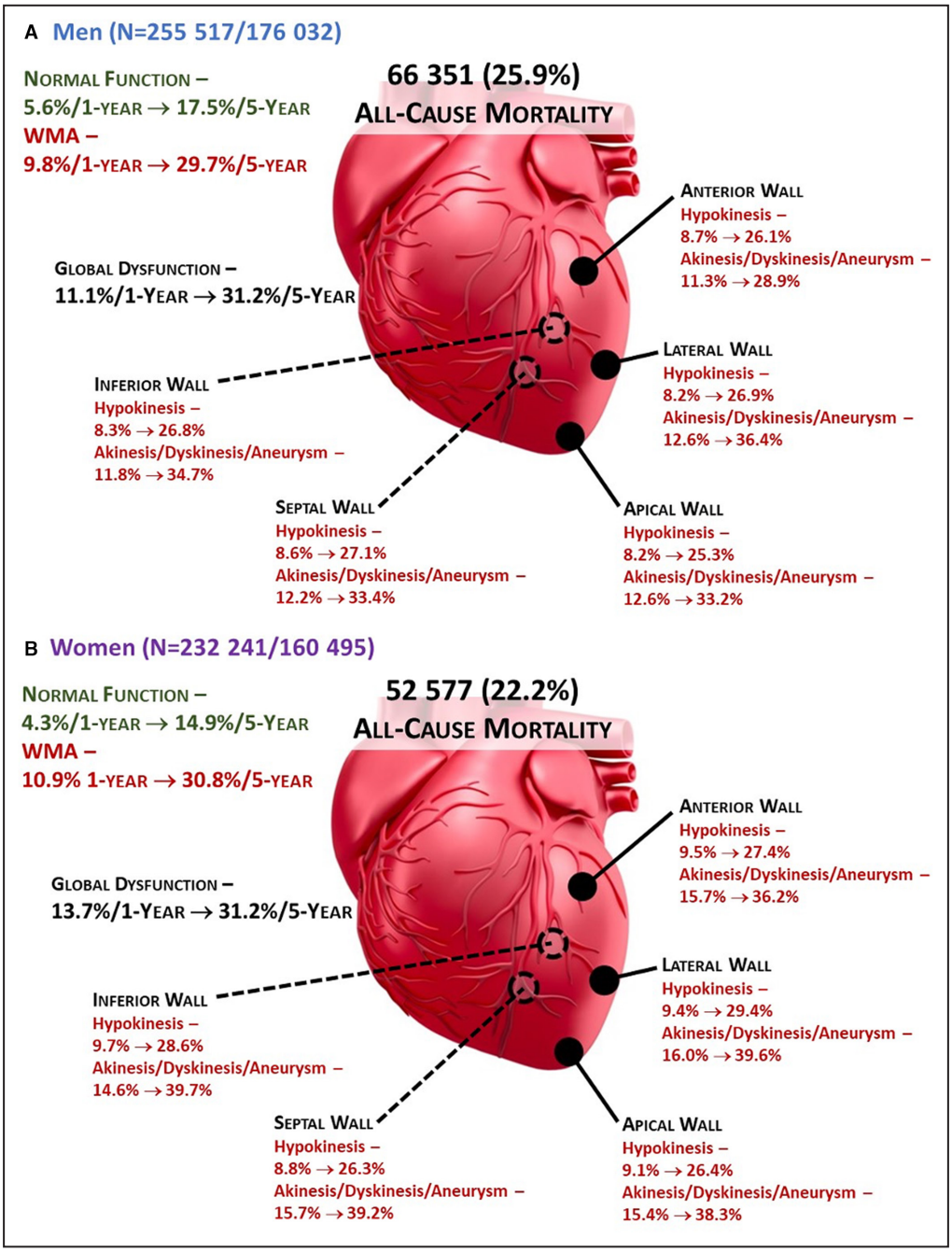

Figure 3. Pattern of actual 1- and 5-year mortality according to wall motion status.
This figure shows the proportion (%) of actual 1-year and 5-year mortality for specific WMA reported among the 251 517 (98.4%) and 176 032 (68.8%) of men (**A**) and 232 241 (98.1%) and 160 495 (67.8%) of women (**B**) with complete 1- and 5-year follow-up from their last echocardiogram to study census, respectively. WMA indicates wall motion abnormality.

findings were consistent; the mortality risk being elevated on an adjusted basis for those with an inferior abnormality (HR, 1.16 [95% CI, 0.99–1.36]; *P*=0.076 and HR, 1.10 [95% CI, 1.03–1.18]; *P*=0.009, respectively) but not so for an anterior abnormality (HR, 0.84 [95% CI, 0.66–1.07]; *P*=0.154 and HR, 0.91 [95% CI, 0.82–1.03]; *P*=0.123, respectively). Similarly, on an adjusted basis, those individuals with septal, lateral, and apical hypokinesis were less likely to die compared with those with other forms of WMA.

DISCUSSION

To our knowledge, this represents the largest real-world multicenter study examining the prevalence,

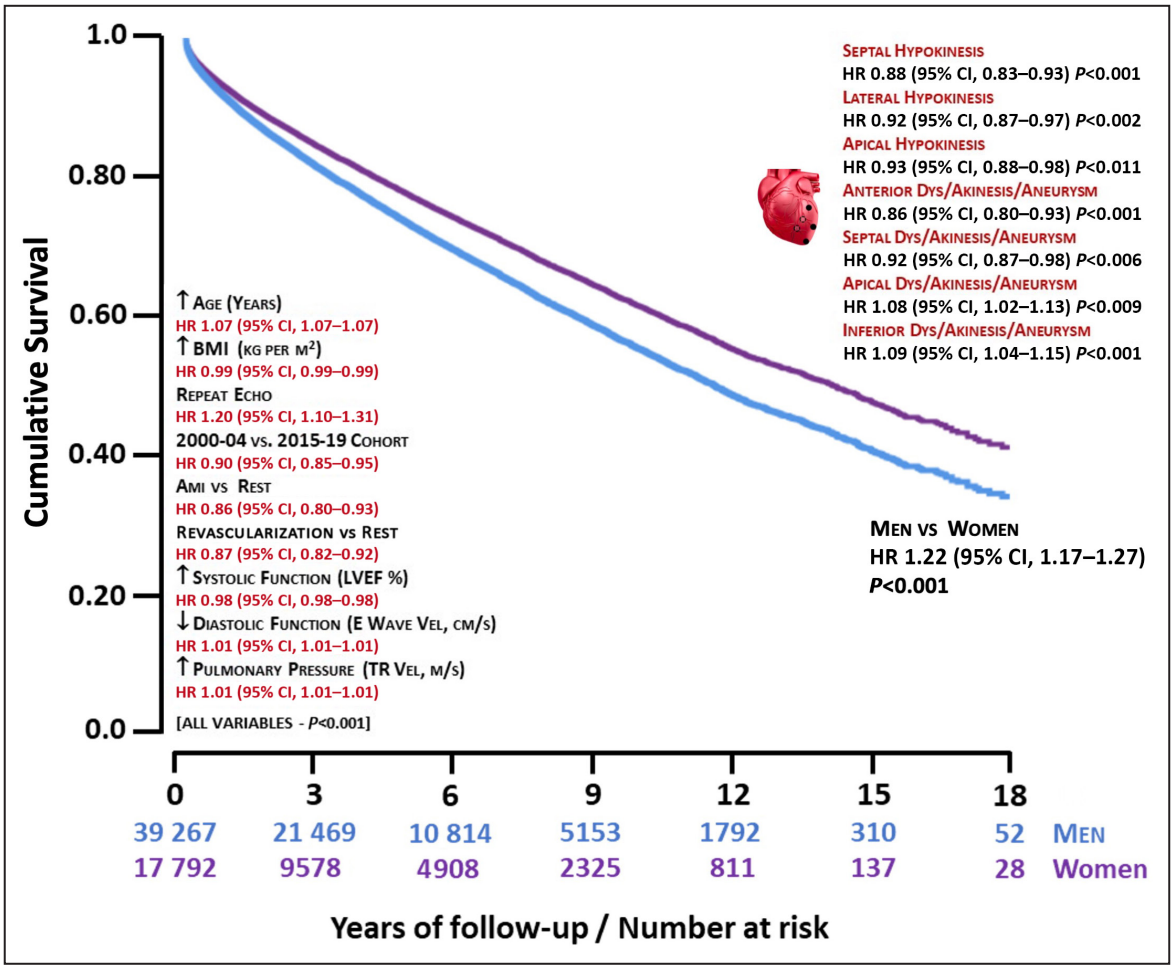

Figure 4. Adjusted risk of mortality according to wall motion status.
This graph compares the adjusted Cox proportional hazard ratio curves for all fatal events in 39267 men and 17792 women included in the model (79 men and 42 women without complete data). All models are visually inspected to assess the proportional hazard assumption. AMI indicates acute myocardial infarction; BMI, body mass index; Dys, dyskinesis; Echo, echocardiogram; HR, hazard ratio; LVEF, left ventricular ejection fraction; and TR, tricuspid regurgitation.

characteristics, and mortality associated with left ventricular RWMA post MI. Overall, we found that twice the number of men than women (15.4% versus 7.5%) were reported to have a WMA. In both men and women, the inferior wall (8.0% and 3.3%, respectively) was most affected and the anterior wall (2.5% and 1.1%, respectively) least affected, with hypokinesis (as opposed to akinesis or dyskinesis) the most common form of abnormality documented. Any reported WMA was more likely in older individuals and those with a prior history of CAD, who had more signs of diastolic dysfunction and pulmonary hypertension, and who were accompanied by a higher risk of subsequent mortality. Global left ventricular dysfunction (with an accompanying fall in left ventricular ejection fraction) was uniformly associated with high 5-year mortality (31.2% in both sexes). In men, but not women, there was a clear differential in 5-year mortality with differing regions involved, with apical, inferior, or lateral wall infarction associated with ~7% higher mortality compared with the anterior wall. Surprisingly, anterior or septal akinesis/dyskinesis/aneurysm was not associated with a higher rate of death. As expected, global LV dysfunction was associated with high rates of mortality, although not as high as some of the more severe, RWMA.

Unadjusted, women with WMA had a higher overall mortality than men, although they were also older in age with more impaired ventricular function. On an adjusted basis, men with WMA were more likely to die, whereas those with a documented AMI or subject to revascularization were less likely to die, consistent with the expected improved outcomes after recognition and treatment of acute coronary ischemic events. A treatment effect may also explain the slightly more favorable survival rates associated with global dysfunction when compared with specific WMAs. A likely treatment effect was also revealed when considering the timing of last echocardiogram (better survival closer to the 2019

census date). As expected, any evidence of adverse left ventricular remodeling (resulting in impaired systolic and diastolic function) was associated with higher mortality.

Echocardiographic RWMA is the commonest echocardiographic manifestation of prior MI,[21,28,29] and when present, increase the risk of subsequent heart failure[29] and confer an adverse prognosis independent of clinical cardiovascular disease and risk factors[30,31] and LVEF.[32] The WMSi has been proposed as an alternative to LVEF post AMI because of the compensation caused by hyperkinesis of the noninfarcted segments.[33–35] However, the WMSi has been predominantly used in research studies (as opposed to clinical practice) due to small sample sizes with insufficient power to examine the prognostic effect of individual WMA.[29] The present study comprising 57 180 individuals (11.6% of the total cohort) with a reported WMA, provides sufficient statistical power to report clinically relevant differences between individual LV regions. Our finding of 15.4% of men and 7.5% of women with a WMA contrasts with the Strong Heart Study and Copenhagen Heart Study (5% of 2864 participants and 2.4% of 3415 participants, respectively),[29,31] both of which examined a population of individuals without known ischemic heart disease at baseline although the higher proportion of WMA in men than women has been consistently demonstrated. Sex differences in AMI presentations parallel the differences observed in our study, with a 3.1-fold higher incidence in men in the United Kingdom,[36] 2.7-fold in Norway,[37] and 1.4-fold in the United States.[38,39] Our demonstration that inferior WMA (most commonly due to right coronary artery territory infarction) is associated with a higher mortality than anterior WMA (left anterior descending territory infarction) has not been addressed in previous studies except in high-risk subgroups,[40] although heart failure outcomes appear similar across individual WMA,[29] and left anterior descending territory (anterior) ischemia on stress echocardiography has a more adverse outcome than other WMA.[41]

Anterior MI has a worse overall prognosis than inferior wall infarction[42,43]; however, progressive improvements in survival after AMI have reflected the success of urgent revascularization[43] and shorter ischemic times.[44] It is possible that the demonstration of a more adverse mortality with inferior WMA in the present study may be due to a survival bias arising from a higher early mortality rate in large anterior MI before echocardiography is performed. It is also possible the observation is due to more frequent use of pharmacological agents to prevent and treat adverse LV remodeling in anterior infarction (such as angiotensin receptor-neprilysin inhibitors,[22] aldosterone receptor antagonists,[18] SGLT-2 antagonists,[19] and beta-blocker therapies[20,21]). Overall, we demonstrated the presence of any WMA increased almost doubled 5-year mortality, consistent with previous studies.[31] Regional WMA may also occur in the absence of obstructive CAD, such as in myocarditis,[45] sarcoidosis,[46] and takotsubo cardiomyopathy,[47] with cardiac conduction abnormalities[48] such as occur with cardiac pacing, left bundle-branch block and prior cardiac surgery, or with right ventricular pressure loading such as observed in pulmonary hypertension. However, each of these disorders is associated with its own mortality trajectory and the observation of WMA, whatever the underlying cause, is an important prognostic factor. Conversely, the absence of WMA does not reassure against the presence of CAD or prior AMI.

The findings of this study have important clinical implications. Despite decreasing frequency of WMA in the modern era (due predominantly to improved early revascularization strategies during AMI), the location, extent, and severity of WMA are prognostically relevant. In particular, women are reported with WMA half as often as their male counterparts, but when present it is associated with a similar 5-year mortality. In addition, identification of RWMAs post MI shows better prediction of 12-month mortality than traditional clinical (such as Thrombolysis in Myocardial Infarction and Global Registry of Acute Coronary Events [GRACE]) scores.[49] As such, assessment of global and regional left ventricular systolic function by echocardiography should be routinely applied in patients undergoing assessment for known or suspected coronary heart disease, and management decisions tailored for the individual based on these findings. Assessment of the adverse prognostic impact of RWMA may be enhanced by the use of machine learning applied to echocardiographic images.[50]

Limitations

Beyond the reliance on 2-dimensional echocardiography, additional associated limitations of using big data have been described previously in other NEDA reports.[51,52] Namely NEDA does not currently capture pharmaceutical use, demographic information (eg, ethnicity or socioeconomic status), or key determinants of health outcomes (eg, CAD, diabetes) outside of the details captured by the National Death Registry of Australia. Furthermore, this cohort typically comprises subjects being investigated for possible or preexisting cardiovascular disease, enriching the population with WMA compared with population-based studies.

Echocardiographic reporting of apical RWMAs varies depending on the nomenclature used by the reporting cardiologist. Although several different segmentation models may be used,[11] we attempted to unify reporting by using only the American Society of Echocardiography and American Heart Association recommended 17-segment model. It is possible that

the 17th segment (true apex) is overrepresented using this approach although the overall results are unchanged. Similarly, although we excluded patients with reported dyssynchrony and cardiac pacing, it is possible some reported RWMA (particularly the ventricular septum) were in fact due to dyssynchronous ventricular contraction and not impaired contractile function, which could partially explain the only modestly impaired survival with septal WMA. In addition, noncoronary causes of WMA (such as myocarditis, takotsubo cardiomyopathy, or dyssynchrony) may have influenced the mortality outcomes, although patients with known dyssynchrony and cardiac pacing were excluded from this analysis. Finally, because of the size and scope of the NEDA data set, we did not perform image review or core-laboratory assessment to independently verify the presence of RWMA, nor did we undertake speckle tracking or contrast echocardiography.

CONCLUSIONS

Regional WMAs following myocardial infarction are reported twice as often in men than in women. Inferior wall motion abnormalities are the most common WMA found, with hypokinesis more common than akinesis, dyskinesis, or aneurysm formation. The presence of WMA is associated with increased mortality, with inferior and apical WMA faring the worst overall, particularly in the presence of dyskinesis, akinesis, or aneurysm formation. Further studies are needed to establish whether the lower frequency of reported WMA in women is due to lower rates of ventricular functional defects following AMI in women, underreporting of WMA due to differences in image quality (and endocardial definition), or possibly whether an unconscious bias exists within reporting physicians. Investigation on whether a change in WMA (improvement, no change, or worsening) affects prognosis. Studies investigating the potential beneficial effect of pharmacotherapy are also needed.

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Disclosures

D.P. is on the advisory board for Echo IQ, Edwards LifeSciences, and AstraZeneca. G.S. is on the advisory board for Echo IQ.

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Supplemental Material

Data S1
Figure S1

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