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Novel adaptation of the KCC-questionnaire for cardiomyopathy screening in a racially diverse obstetric population

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Cardiomyopathy occurring during pregnancy or postpartum represents a leading cause of maternal mortality. An overlap between pregnancy-associated symptoms and symptoms of cardiomyopathy contributes to delays in diagnosis. To address the need for screening and improve the diagnosis of pregnancy-related cardiomyopathy, we sought to evaluate the association between cardiovascular symptoms, an adapted version of the 12-item Kansas City Cardiomyopathy Questionnaire for pregnancy (KCCQ-P) and left ventricular systolic dysfunction (LVSD). We conducted a single-arm prospective observational study of pregnant and postpartum participants enrolled between October 2021 and October 2022. A symptom questionnaire, KCCQ-P, and a resting echocardiogram were performed. The primary study outcome was LVSD, defined as left ventricular ejection fraction (LVEF) < 50%. We sub-divided those with LVEF (≥50%) into subclinical LVSD (left ventricular global longitudinal strain (GLS) > −18), and no LVSD (GLS ≤ −18). Ninety women were included in the final analysis. The median age was 31 years (Q1: 28, Q3: 35), 37% identified as Non-Hispanic White, 30% as Non-Hispanic Black, and 23% as Hispanic or Latino. KCCQ-P total scores were markedly lower with LVSD (median: 30.2; Q1: 22.9, Q3: 61.5) vs. subclinical LVSD (median: 60.7; Q1: 47.0, Q3: 76.2) vs. no LVSD (median: 86.5; Q1: 62.5, Q3: 95.8) $p < 0.001$. KCCQ-P score was able to detect LVSD with an AUC of 0.848. While individual cardiovascular symptoms were not associated with LVSD, KCCQ-P scores were significantly lower in those with apparent and subclinical LVSD and may be useful as a screening tool pending additional evaluation in larger cohorts.

INTRODUCTION

The United States is the only industrialized nation with a rising maternal mortality rate which has been increasing over the past 3 decades[1–4] with Black women having a 2–3 fold higher risk over their White counterparts[5,6]. Even more concerning, maternal mortality review committees have found that the majority (up to 80%) of these deaths are preventable[5,7]. The prevalence of cardiovascular-related morbidity during pregnancy has also increased due to multiple factors including older age at first pregnancy, higher burden of preexisting cardiovascular risk factors (diabetes, hypertension, obesity, smoking), and increasing numbers of women of reproductive age living with congenital heart disease[8]. Based on data from the U.S. National Inpatient Sample, the prevalence of cardiovascular disease among pregnant individuals at the time of delivery increased by 24.7% from 2003 to 2012[9] with similar increases in severe cardiovascular maternal morbidity from 1999 through 2015[10].

Cardiomyopathy is a primary contributor to pregnancy-related cardiovascular morbidity and mortality[6]. In 2016–2017, cardiomyopathy was the second leading cause of death during and through 6 weeks after delivery for Non-Hispanic Black women and was the number one cause of late maternal deaths (43 days to 1 year) for all women[11]. Peripartum cardiomyopathy (PPCM) is a unique form of pregnancy-related cardiomyopathy characterized by left ventricular systolic dysfunction, that occurs towards the end of pregnancy and the postpartum period with up to a 16-fold higher prevalence among Black women[12]. Because the cardinal symptoms of cardiomyopathy (shortness of breath, fatigue, and lower extremity edema) are also common in pregnancy, identifying pregnant individuals with cardiomyopathy can be delayed, resulting in worse outcomes and death[13,14]. To help address the need for more efficient recognition of pregnancy-related cardiomyopathy, better methods for risk-stratifying pregnant and postpartum individuals for additional testing (e.g., echocardiography) are desperately needed. While a cardiovascular disease screening toolkit has been developed by the California Maternal Quality Care Collaborative (CMQCC)[15] and endorsed by the American College of Obstetrics and Gynecology[16] to facilitate the recognition of cardiovascular disease during pregnancy, the algorithm is data intensive and currently not validated[17].

The Kansas City Cardiomyopathy Questionnaire (KCCQ) is a validated and reliable tool used to evaluate health status among patients with heart failure[18,19], but has not been evaluated during pregnancy. We hypothesized that its ability to better stratify the range of heart failure symptoms might distinguish underlying cardiac dysfunction from the less severe symptoms of normal pregnancy. Our study objective was to conduct a prospective observational study to compare the effectiveness of a pregnancy-adapted version of the 12-item KCCQ (KCCQ-P) with individual

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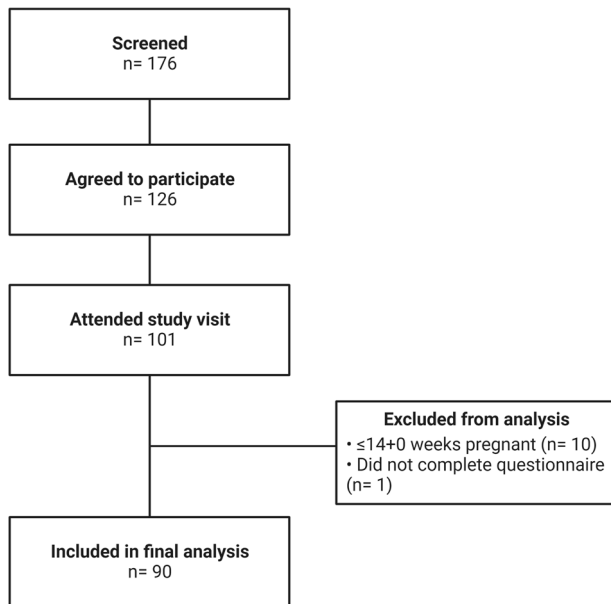
Fig. 1 Study flow diagram. We evaluated 126 consenting pregnant and postpartum women aged ≥18 years, of which 101 attended their study visit. Women ≤14 weeks + 0 of gestation or with a history of complex congenital heart disease or significant conduction abnormalities were excluded. Ninety study participants completed all study-related testing and questionnaires and were included in the final analysis.

cardiovascular symptoms and risk factors in detecting echocardiographic evidence of left ventricular systolic dysfunction (LVSD) in an obstetric population.

METHODS

We conducted a prospective, single-arm, observational study among pregnant and postpartum individuals. The study was approved by the Mayo Clinic Institutional Review Board, and we followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Study setting

Study participants were recruited from 3 sites: Mayo Clinic Jacksonville, Florida, Agape Family Health Clinic, Jacksonville, Florida, and Mayo Clinic Rochester, Minnesota. We included individuals seen for obstetric care at a prenatal clinic, any routine clinical care, hospital staff, and self-referred participants who voluntarily agreed to participate in the study between October 28 2021 and October 27, 2022.

Participants and study procedures

Sex, race, and gender identity were obtained on all study participants using a self-administered questionnaire. All study participants identified as female and, as such, all participants are referred to as women throughout the manuscript. We evaluated 126 consenting pregnant and postpartum women aged 18 and older. Pregnancy and postpartum status were self-reported by all participants. Women at ≤14 weeks + 0 of gestation were excluded as cardiovascular symptoms experienced during early normal pregnancy are known to be infrequent or less severe than that seen later in pregnancy[12,13,20]. In addition, peak hemodynamic changes occur in the second trimester and heart failure symptoms often manifest during this period among women with pre-existing heart disease[12]. We also excluded patients with a history of complex congenital heart disease (including complex cardiac

surgery, single ventricle physiology, or significant shunts with cardiac structural abnormalities) or significant conduction abnormalities (ventricular pacing on a recorded ECG, or pacemaker dependence). Ninety study participants who were at >14 weeks + 0 of gestation or postpartum (up to 12 months post-delivery), completed all study-related testing, and questionnaires were included in the final analysis (Fig. 1). The baseline questionnaire included demographic questions, medical history, heart failure symptoms from the CMQCC toolkit (dyspnea, orthopnea, tachypnea, and episodes of 'asthma' that did not improve with inhalers or other treatment), social determinants of health (educational level, marital status, employment status, health care coverage, and access to a physician), and an assessment of health status using the KCCQ-P. Study participants were followed up at approximately 3-month intervals through 12 months postpartum or end of study period, depending on which was earlier. Repeat questionnaires were administered during follow-up visits and medical records were reviewed. Results from questionnaire data gathered at the baseline visit only are reported in this manuscript. Consent forms and questionnaires were made available in English and Spanish. However, all study participants opted to complete the English version of the questionnaires. Study coordinators who recruited Hispanic participants were bilingual, and fluent in English and Spanish and provided additional translation support as needed.

Creation of the KCCQ-P

The KCCQ was developed in 2000 as a disease-specific health status measure for patients with heart failure. Originally developed as a 23-item questionnaire, the KCCQ provides disease-specific assessments of physical limitation, symptoms (frequency, severity, and recent change over time), quality of life, social limitations, and self-efficacy[18]. In 2015, a shorter version of the KCCQ consisting of only 12-items (KCCQ-12) was shown to be highly correlated with the original KCCQ scores, and to preserve its validity, reliability, and prognostic properties[19]. KCCQ scores range from 0 to 100 and can be interpreted as follows: 0 to 24 (very poor to poor health status); 25 to 49 (poor to fair health status); 50 to 74 (fair to good health status); and 75 to 100 (good to excellent health status)[21]. The KCCQ-12 questionnaire includes 8 sections with graded responses. Given that the KCCQ-12 was designed as a disease-specific health status measure for patients with heart failure, it required adaptation for a population of pregnant women. In collaboration with the instrument's developer, changes to the descriptive stems of the questionnaire were made. These included replacing the term 'heart failure' with 'during pregnancy', 'heart failure symptoms' with 'pregnancy symptoms', and 'symptoms of heart failure' with 'these symptoms (shortness of breath/fatigue)' (Supplemental Material).

Assessments of cardiac function

Questionnaires were completed on the same day prior to, or immediately following resting transthoracic echocardiogram image acquisition, with assessments of left ventricular ejection fraction (LVEF) and left ventricular global longitudinal systolic strain (GLS). Final echocardiogram results were not available to participants before questionnaire completion except for one participant who had questionnaires completed 24 hours following a clinical echocardiogram. LVEF and GLS were assessed by board-certified cardiologists based on the American Society of Echocardiography guidelines[22], with all images obtained by trained sonographers at Mayo Clinic using standard transthoracic imaging protocols. LVEF was assessed using standard methods with Simpson's biplane method of disks >> 2D linear (modified Quinones method) >> M-mode >> visual assessment in this order of priority based on image quality.

Table 1. Baseline Demographics and Clinical Characteristics of the Study Sample.

	No LVSD (LVEF ≥ 50%, GLS ≤ −18%) n = 69	Subclinical LVSD (LVEF ≥ 50%, GLS > −18%) n = 16	LVSD (LVEF < 50%) n = 5	Overall n = 90	p value
Age (years)[a]	31.76 (29.12, 34.99)	27.68 (21.51, 32.54)	28.33 (24.64, 33.41)	31.67 (28.35, 34.79)	0.104
BMI (kg/m^2)[a]	28.04 (23.13, 30.83)	33.32 (31.06, 40.16)	28.34 (24.44, 28.36)	28.78 (24.44, 32.84)	0.003
Race/Ethnicity					0.158
Non-Hispanic White	28 (40.58%)	2 (12.5%)	3 (60.0%)	33 (36.67%)	
Non-Hispanic Black or African American	17 (24.64%)	8 (50.0%)	2 (40.0%)	27 (30.0%)	
Hispanic or Latino	17 (24.64%)	4 (25.0%)	0 (0%)	21 (23.33%)	
Asian	5 (7.25%)	1 (6.25%)	0 (0%)	6 (6.67%)	
Multi-racial	2 (2.9%)	0 (0%)	0 (0%)	2 (2.22%)	
Native Hawaiian/Pacific Islander	0 (0%)	1 (6.25%)	0 (0%)	1 (1.11%)	
Recruitment Site					0.036
Mayo Clinic Florida	36 (52.17%)	5 (31.25%)	4 (80.0%)	45 (50.0%)	
AGAPE Clinic	27 (39.13%)	11 (68.75%)	0 (0%)	38 (42.22%)	
Mayo Clinic Rochester	6 (8.7%)	0 (0%)	1 (20.0%)	7 (7.78%)	
Pregnant or Postpartum					0.006
Pregnant	52 (75.36%)	15 (93.75%)	1 (20.0%)	68 (75.56%)	
Postpartum (within 12 months)	17 (24.64%)	1 (6.25%)	4 (80.0%)	22 (24.44%)	
Systolic Blood pressure (mmHg)[a]	112.00 (104.00, 118.00)	119.00 (114.50, 124.00)	115.00 (97.00, 119.00)	113.00 (104.25, 120.00)	0.099
Systolic Blood Pressure > 140					1.0
No	67 (97.1%)	16 (100.0%)	5 (100.0%)	88 (97.78%)	
Yes	2 (2.9%)	0 (0%)	0 (0%)	2 (2.22%)	
Diastolic blood pressure[a]	70.00 (64.00, 76.00)	72.50 (67.25, 75.00)	74.00 (63.00, 77.00)	70.00 (64.00, 75.75)	0.711
Heart rate (beats per minute)[a]	73.00 (67.00, 83.00)	85.50 (81.00, 90.75)	100.00 (97.00, 112.00)	76.00 (68.25, 86.75)	<0.001
Heart rate >110 beats per minute					0.007
No	69 (100.0%)	15 (93.75%)	3 (60.0%)	87 (96.67%)	
Yes	0 (0%)	1 (6.25%)	2 (40.0%)	3 (3.33%)	
Education Level					1.0
Less than high school	8 (11.59%)	1 (6.25%)	0 (0%)	9 (10.0%)	
High school or GED	11 (15.94%)	9 (56.25%)	1 (20.0%)	21 (23.33%)	
Some college	11 (15.94%)	1 (6.25%)	1 (20.0%)	13 (14.44%)	
Bachelor's degree or higher	38 (55.07%)	5 (31.25%)	3 (60.0%)	46 (51.11%)	
Employment Status					0.043
Employed full or part-time	50 (72.46%)	6 (37.5%)	4 (80.0%)	60 (66.67%)	
Unemployed/unable to work/ retired	12 (17.39%)	8 (50.0%)	0 (0%)	20 (22.22%)	
Homemaker	4 (5.8%)	1 (6.25%)	1 (20.0%)	6 (6.67%)	
Student	3 (4.35%)	1 (6.25%)	0 (0%)	4 (4.44%)	
Marital Status					0.448
Married/cohabitating	46 (66.67%)	8 (50.0%)	4 (80.0%)	58 (64.44%)	
Separated/divorced/widowed	9 (13.04%)	2 (12.5%)	1 (20.0%)	12 (13.33%)	
Single/never married	1 (1.45%)	1 (6.25%)	0 (0%)	2 (2.22%)	
Had children prior to index pregnancy?	48 (69.57%)	9 (56.25%)	5 (100.0%)	62 (68.89%)	0.208
Have healthcare coverage? (Yes)	57 (82.61%)	13 (81.25%)	5 (100.0%)	75 (83.33%)	0.591
Have a primary care provider? (Yes)	53 (76.81%)	12 (75.0%)	4 (80.0%)	69 (76.67%)	0.608
Unable to see a doctor in the past year	9 (13.04%)	3 (18.75%)	0 (0%)	12 (13.33%)	0.238
Reported Symptoms					
Dyspnea	43 (62.32%)	10 (62.5%)	5 (100.0%)	58 (64.44%)	0.296
Orthopnea	35 (50.72%)	11 (68.75%)	5 (100.0%)	51 (56.67%)	0.061

Table 1 continued

	No LVSD (LVEF ≥ 50%, GLS ≤ −18%) n = 69	Subclinical LVSD (LVEF ≥ 50%, GLS > −18%) n = 16	LVSD (LVEF < 50%) n = 5	Overall n = 90	p value
Tachypnea	28 (40.58%)	9 (56.25%)	3 (60.0%)	40 (44.44%)	0.584
Episode of 'asthma' unresponsive to therapy	2 (2.9%)	0 (0%)	1 (20.0%)	3 (3.33%)	0.202
Echocardiographic Measures					
LV mass index (g/m2)[a]	73.00 (61.00, 80.00)	74.00 (61.25, 82.25)	96.00 (83.00, 101.00)	74.00 (62.25, 81.75)	0.093
LV relative wall thickness (%)[a]	37.00 (33.00, 42.00)	42.50 (35.75, 43.25)	28.00 (26.00, 28.00)	37.00 (33.00, 42.00)	0.001
LV end diastolic diameter (mm)[a]	45.00 (43.00, 49.00)	46.00 (43.00, 48.25)	58.00 (57.00, 62.00)	46.00 (43.00, 50.00)	0.001
LV end-systolic diameter (mm)[a]	30.00 (27.00, 33.00)	30.00 (27.75, 33.25)	50.00 (49.00, 58.00)	30.00 (28.00, 33.00)	0.001
Mitral valve E/e' ratio[a]	7.40 (6.40, 8.90)	8.35 (6.38, 10.00)	14.95 (10.98, 20.83)	7.80 (6.40, 9.10)	0.008
Mitral valve E/e' ratio > 15					0.013
No	68 (98.55%)	16 (100.0%)	3 (60.0%)	87 (96.67%)	
Yes	1 (1.45%)	0 (0%)	2 (40.0%)	3 (3.33%)	
LV global longitudinal systolic strain[a]	−20.00 (−21.00, −19.00)	−16.50 (−17.00, −15.00)	−10.00 (−11.50, −7.50)	−19.00 (−21.00, −18.00)	<0.001
Cardiac output - Doppler method (L/min)[a]	5.52 (4.63, 6.09)	6.04 (5.62, 6.50)	5.49 (4.89, 5.56)	5.56 (4.82, 6.22)	0.087
Cardiac index (L/min/m²)[a]	3.01 (2.63, 3.38)	2.87 (2.71, 3.25)	2.83 (2.64, 2.91)	2.92 (2.65, 3.36)	0.678
Peak tricuspid regurgitation velocity (m/s)[a]	2.13 (1.83, 2.26)	2.25 (2.04, 2.31)	2.94 (2.66, 3.12)	2.16 (1.84, 2.30)	0.019
Left atrial volume index (ml/m²)[a]	26.00 (22.00, 29.50)	22.50 (20.75, 26.25)	27.00 (24.00, 28.75)	25.00 (22.00, 29.00)	0.273
Right atrial volume index (ml/m²)[a]	20.05 (15.10, 23.98)	15.55 (13.32, 19.25)	16.50 (14.00, 29.00)	18.90 (15.00, 23.15)	0.114
LV geometry					0.014
Normal geometry	47 (68.12%)	7 (43.75%)	2 (40.0%)	56 (62.22%)	
Concentric remodeling	14 (20.29%)	8 (50.0%)	0 (0%)	22 (24.44%)	
Eccentric hypertrophy	7 (10.14%)	1 (6.25%)	3 (60.0%)	11 (12.22%)	
Concentric hypertrophy	1 (1.45%)	0 (0%)	0 (0%)	1 (1.11%)	
Diastolic function					0.003
Normal	65 (94.2%)	14 (87.5%)	2 (40.0%)	81 (90.0%)	
Abnormal	3 (4.35%)	0 (0%)	1 (20.0%)	4 (4.44%)	
Indeterminate	1 (1.45%)	2 (12.5%)	2 (40.0%)	5 (5.56%)	
Comorbid Conditions					
Chronic hypertension	3 (4.35%)	0 (0%)	0 (0%)	3 (3.33%)	1.0
Gestational hypertension	1 (1.45%)	0 (0%)	2 (40.0%)	3 (3.33%)	0.017
Preeclampsia	2 (2.9%)	0 (0%)	2 (40.0%)	4 (4.44%)	0.016
Gestational diabetes	2 (2.9%)	2 (12.5%)	2 (40.0%)	6 (6.67%)	0.008
Small for gestational age baby	2 (2.9%)	1 (6.25%)	0 (0%)	3 (3.33%)	0.554
Preterm birth	1 (1.45%)	0 (0%)	1 (20.0%)	2 (2.22%)	0.139
Pregnancy Outcome					0.027
Livebirth (single)	58 (84.06%)	13 (81.25%)	4 (80.0%)	75 (83.33%)	
Livebirth (multiple)	0 (0%)	1 (6.25%)	1 (20.0%)	2 (2.22%)	

[a]Median and interquartile range reported.
BMI Body mass index, *GED* General Educational Development Test, *GLS* Global longitudinal systolic strain, *LV* Left ventricle, *LVEF* Left ventricular ejection fraction, *LVSD* Left ventricular systolic dysfunction.

Outcomes
The primary outcome of interest was LVSD, defined as a left ventricular ejection fraction (LVEF) < 50% using standard 2-D echocardiography. To evaluate the potential differences in symptoms and KCCQ-P scores across a broader spectrum of cardiovascular dysfunction (apparent and subclinical), we conducted a secondary analysis by classifying participants as having LVSD (LVEF < 50%), subclinical LVSD (LVEF ≥ 50% and GLS > −18%[23,24]), or no LVSD (LVEF ≥ 50% GLS ≤ −18). Three participants with LVEF ≥ 50% were unable to have strain performed due to image quality and these were assumed to have normal GLS based on the median GLS value for the entire cohort.

Statistical analysis
As part of a preliminary analysis, the internal consistency of the KCCQ-P, using the same scoring approach as the KCCQ-12, was

assessed using Cronbach's alpha. Upon confirming adequate internal reliability of the KCCQ-P, additional analyses were conducted.

The main predictor of interest was the KCCQ-P score. To define the relationship of KCCQ-P with LVSD, a Receiver Operating Characteristic (ROC) analysis was conducted using the KCCQ-P as the discriminator. An optimal cut-point was selected based on Youden's index, and subsequently, standard measures of diagnostic performance, including the diagnostic odds ratio[25], and associated 95% CIs were computed. To further explore the association of KCCQ-P in the secondary analysis with the trichotomous LVSD classification, ordinal logistic regression (proportional odds model) was employed to estimate the common (or pooled) diagnostic odds ratio. The number of LVSD cases was less than 10[26], so adjusted analyses were not performed. As an alternative, descriptive statistics were tabulated across the LVSD classifications. Variables evaluated included demographics, medical history (reported by the patient or abstracted from electronic medical records when available), cardiovascular symptoms, heart rate, blood pressure, and social determinants of health. Continuous variables across the 3 groups of cardiac function were summarized as median and interquartile range and categorical variables as frequencies and percentages to describe the profile of the population. Fisher's exact (for categorical variables), and Kruskal-Wallis tests (for numeric variables) were employed to evaluate the association between LVSD classes and the patient variables. A p value < 0.05 was considered statistically significant. All analyses were performed using R version 3.5.2 (Vienna, Austria) and Python version 3.9.7.

RESULTS

Table 1 shows baseline demographic and clinical characteristics of our study sample. The median age was 31 years (Q1:27, Q3:34), 76% were pregnant and 24% postpartum at the time of enrollment. Thirty-seven percent identified as Non-Hispanic White, 30% as Non-Hispanic Black, 23% as Hispanic or Latino, 7% as Non-Hispanic Asian, 2% as Multiracial, and 1% as Native Hawaiian/ Pacific Islander. Six percent had LVSD (LVEF < 50%), 18% had subclinical LVSD, and 76% had normal left ventricular systolic function (no LVSD). There were significant differences in BMI, enrollment site, postpartum status, heart rate, employment status, hypertensive disorders of pregnancy, gestational diabetes, and pregnancy outcome across LVSD subgroups. Social determinants of health including educational level, marital status, and health care coverage were not statistically different across sub-groups. Resting heart rate, left ventricular end-diastolic dimension, left ventricular end-systolic dimension, and E/e' ratio (determined by spectral Doppler of the mitral inflow velocity and tissue Doppler velocity of medial mitral annular early-diastolic excursion) were higher among women with LVEF < 50% compared with those having an LVEF ≥ 50%. Cardiovascular symptoms including dyspnea, orthopnea, and tachypnea were reported in 64%, 57%, and 44% of all participants respectively. Other than HR > 110 bpm, heart failure symptoms (dyspnea, orthopnea, tachypnea, asthma unresponsive to therapy), vital signs (SBP > 140 mmHg), and risk factors (age ≥ 40, Black race, chronic hypertension) included in the ACOG recommended CMQCC toolkit screening algorithm[15] were not significantly different across LVSD groups.

Internal consistency of the KCCQ-P
The KCCQ-P had high internal consistency with a Cronbach's alpha of 0.81 for Physical Limitation, 0.78 for Symptom Frequency, 0.74 for Social Limitations (0.740) and 0.93 for the Quality of Life scales. The internal consistency of the Overall Summary Score was 0.930.

The association of KCCQ-P scores with LVSD
KCCQ-P scores were significantly lower among women with LVEF < 50% (median 30.2; Q1: 22.9, Q3: 61.5) than in women with LVEF ≥ 50% (median 82.3; Q1: 59.4, Q3: 93.8; $p = 0.009$) than in women with LVEF ≥ 50% (median 82.3; Q1: 59.4, Q3: 93.8; $p = 0.009$). In the subgroup of women with LVEF ≥ 50%, the KCCQ-P was also significantly lower in those with subclinical LVSD (median 60.7; Q1: 47.0, Q3: 76.2) than in those without LVSD (median 86.5; Q1: 62.5, Q3: 95.8; $p = 0.01$). This analysis showed a linear relationship between KCCQ-P scores and LVSD subgroups (Spearman's correlation coefficient $p < 0.001$, Table 2).

The use of the KCCQ-P score alone was able to detect LVSD with an AUC of 0.848 (95% CI: 0.711 to 0.986) Fig. 2A. At an optimal cut-point value of 65.625 based on the Youden's index, KCCQ-P provided a classification accuracy of 87.8% (79/90; 95% CI: 79.2% to 93.7%), sensitivity of 60% (3/5; 95% CI: 14.7% to 94.7%), specificity of 89.4% (76/85; 95% CI: 80.8% to 95.0%), positive predictive value of 25.0% (3/12; 95% CI: 5.5% to 57.2%), and negative predictive value of 97.4% (76/78; 95% CI: 91.0% to 99.7%) Fig. 2B. We also evaluated alternate cut-points for the KCCQ-P score if a higher sensitivity or specificity is desired (Supplemental Table 1). For the ordinal classification of no LVSD ($n = 69$), subclinical LVSD ($n = 16$), and LVSD ($n = 5$), for each 10 unit decrease in the KCCQ-P score (i.e., worse score), the common diagnostic odds ratio for having more severe LVSD increased by 40% (common diagnostic OR 1.40, 95% CI: 1.16 to 1.73; $p < 0.001$). Using the threshold of KCCQ-P score <= 65, the common diagnostic odds ratio estimate was 5.80 (95% CI: 2.09 to 17.4; $p < 0.001$).

DISCUSSION
Given the rising maternal mortality rates in the US, and the fact that cardiomyopathy is a leading cause of death, identifying high-risk pregnant and post-partum individuals for additional cardiovascular assessments (e.g., echocardiography) to diagnose LVSD remains a critical challenge in current care. In this study, we found that simply assessing the presence of cardiovascular symptoms did not discriminate the severity of cardiac dysfunction, as these symptoms occur frequently during pregnancy. Other than heart rate, clinical signs, and risk factors also did not effectively identify the presence of LVSD. In contrast, we found a strong association between KCCQ-P scores and LVSD subgroups (apparent and subclinical) in a racially diverse sample of pregnant and postpartum women (Fig. 3). The findings from our study suggest that a novel adaptation of an existing cardiomyopathy questionnaire might be useful in screening obstetric patients.

Given the importance of early detection and diagnosis of cardiomyopathy during pregnancy, prior efforts have sought to develop a cost-effective and scalable screening tool to identify high-risk pregnant individuals who warrant additional evaluation. Current recommendations for identifying high-risk women are based on the CMQCC toolkit developed in 2017[15] from a small sample of patients ($n = 64$)[14] for cardiovascular (CV) risk assessment among pregnant and postpartum individuals. This toolkit proposes an algorithmic approach evaluating a combination of pre-specified variables[15] and has been endorsed by the American College of Obstetrics and Gynecology[16]. It recommends a combination of patient reported symptoms, vital signs, risk factors, and physical examination findings prior to cardiovascular testing or referral. A recent prospective study evaluating the performance of this algorithm among 834 obstetric patients (after excluding those with known CVD)[27] had a positive predictive value of approximately 30%, with the assumption that all patients who screened negative did not have cardiovascular disease as no further cardiovascular evaluation was performed in that group. In addition, only 2.3% of the study sample had echocardiography performed[27]. However, the relationship between the CMQCC

Table 2. KCCQ-P Score Stratified by Left Ventricular Systolic Dysfunction (LVSD) Subgroups.

	No LVSD (LVEF ≥ 50%, GLS ≤ −18%)	Subclinical LVSD (LVEF ≥ 50%, GLS > −18%)	LVSD (LVEF < 50%)	Overall	p value
KCCQ-P score (n = 90)	86.46 (62.50, 95.83)	60.68 (47.01, 76.17)	30.21 (22.92, 61.46)	78.12 (56.90, 92.71)	<0.001
KCCQ-P Physical limitation score (n = 89)	83.33 (66.67, 100.00)	58.33 (50.00, 75.00)	50.00 (41.67, 66.67)	83.33 (58.33, 91.67)	<0.001
KCCQ-P Symptom frequency score (n = 90)	85.42 (75.00, 100.00)	61.46 (45.31, 79.69)	25.00 (4.17, 50.00)	81.25 (54.17, 98.96)	0.002
KCCQ-P Quality of life score (n = 90)	75.00 (50.00, 100.00)	50.00 (46.88, 75.00)	12.50 (0.00, 37.50)	62.50 (40.62, 100.00)	0.001
KCCQ-P Social limitation score (n = 85)	91.67 (66.67, 100.00)	66.67 (45.83, 79.17)	58.33 (25.00, 66.67)	83.33 (58.33, 100.00)	<0.001

GLS Global longitudinal systolic strain, KCCQ-P Pregnancy adapted version of the 12-item Kansas City Cardiomyopathy Questionnaire, LVEF Left ventricular ejection fraction, LVSD Left ventricular systolic dysfunction.

toolkit variables and LVSD specifically have not previously been described. In this study, we found 64% of study participants endorsed dyspnea, 57% endorsed orthopnea, 44% reported tachypnea and 3% reported episodes of "asthma" unresponsive to therapy. Other than heart rate, other CMQCC toolkit variables including systolic BP ≥ 140 mmHg, age ≥40 years, Black race, and BMI ≥ 35 were not significantly associated with LVSD. As such, it is possible that the use of the CMQCC toolkit alone for cardiomyopathy screening may not identify all high-risk women. In contrast, the KCCQ-P was strongly associated with LVSD with an AUC of 0.85, a positive predictive value of 25% and a negative predictive value of >97%. While it is not clear why the KCCQ-P was so much more discriminative than symptoms alone, we suspect that it is due to its ability to stratify a much broader range of symptom severity than the current toolkit, which only classifies the symptoms as being present or not.

Congruent with the findings in this study, Germain et al. noted that commonly reported symptoms during pregnancy include palpitations, fatigue, decreased exercise tolerance, presyncope/syncope, shortness of breath (occurring in up to 70% of women) and ankle swelling (in up to 80% of women in late pregnancy)[13]. In addition, clinical signs commonly associated with pregnancy may also be seen with cardiovascular conditions and these include sinus tachycardia, splitting of the second heart sound (S2), a third heart sound (S3) and an ejection systolic murmur[13]. The severity of pregnancy related symptoms typically worsens as pregnancy progresses, peaking during the 3rd trimester or late pregnancy which also coincides with the time period that heart failure is likely to occur during pregnancy[28], however the postpartum period is also a high risk window for heart failure occurrence[29]. Although LVSD was more common in postpartum women, we observed that the frequency of symptoms remained high among postpartum women with normal LVEF (n = 18) with 67% reporting dyspnea, 50% reporting orthopnea, and 39% reporting tachypnea. Additional factors that might contribute to delayed identification and care in the postpartum period includes limited interaction (single clinic visit at 6 weeks) with a health care professional in the postpartum period, potential misdiagnosis of symptoms (often misdiagnosed as anxiety or asthma[30]), and loss to follow up. Previously identified reasons for loss to follow up include low attendance at the 6-week postpartum visit[31,32], lack of healthcare coverage beyond 6 weeks postpartum, and caregiver responsibilities (other children, as well as the newborn infant)[33] making it challenging for postpartum individuals to seek care or attend traditional, in-person clinic visits.

This study also examined a spectrum of cardiac dysfunction, including those with sub-clinical LVSD as assessed by abnormal GLS in the setting of a preserved LVEF. Although the clinical implications of subclinical LVSD based on GLS in the obstetric population remains unclear, there is evidence that GLS is a better reflection of LV systolic function than ejection fraction alone and with incremental prognostic value above and independent of ejection fraction[34]. In addition, previous studies have demonstrated that women with hypertensive disorders of pregnancy[35] and women who subsequently developed PPCM[36] have abnormal GLS on echocardiography. These suggest that GLS might be a useful metric for detecting subclinical cardiac dysfunction in pregnancy.

Among Black women, cardiomyopathy and hypertensive disorders are the leading causes of maternal deaths with mortality rates due to cardiomyopathy being 5 times higher for Black women than White women[11]. Cardiomyopathy is also the leading cause of late maternal deaths among all women in the U.S[6,11]. The incidence and prevalence of any cardiomyopathy with left ventricular dysfunction among pregnant or reproductive-age women in the United States is unknown, however international studies in predominantly Black populations have reported an incidence of one per 299 livebirths[37] and prevalence rates as high as 6–10% in the pregnant and postpartum period[38]. The incidence
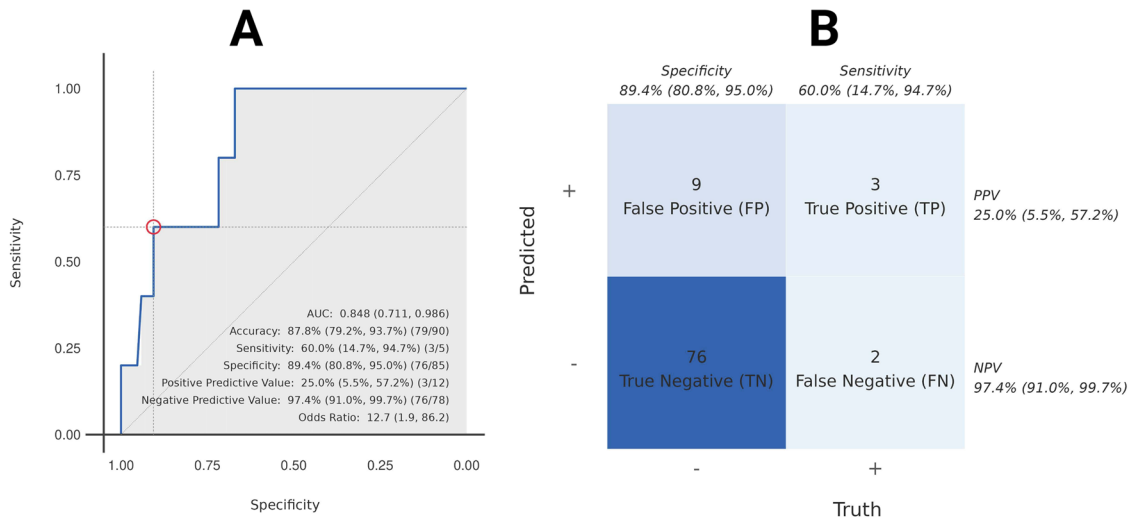
Fig. 2 Receiver operating characteristic (ROC) curve and confusion matrix. A shows the ROC curve and **B** shows the confusion matrix for detection of left ventricular systolic dysfunction (LVEF <50%) using the KCCQ-P score alone (an optimal cut-point value of 65.625 based on the Youden's index) among pregnant and postpartum women.
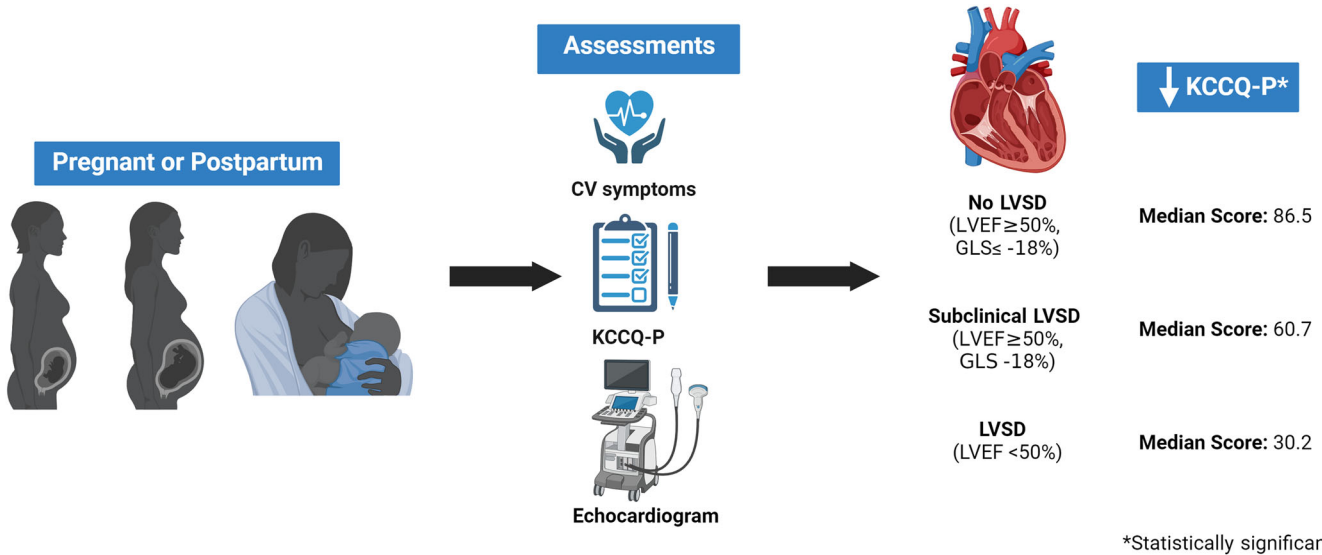

Fig. 3 Novel Adaptation of the KCC-Questionnaire for Cardiomyopathy Screening in a Racially Diverse Obstetric Population. We demonstrate statistically significant differences in KCCQ-P summary scores across left ventricular systolic dysfunction (LVSD) subgroups.

of PPCM is estimated to be 1 in 1000–4000 deliveries in the U.S[12]., although PPCM rates are reported to be up to 16 times more common among Black women compared to White women[12]. In addition, Black patients with PPCM often present later, have poorer outcomes, and lower rates of myocardial recovery, than White patients according to data from the IPAC trial[39]. Currently, screening for cardiomyopathy is not included as part of routine obstetric care and remains an unmet need given its association with maternal morbidity and mortality, as well as previous studies identifying delays in diagnosis to be a significant contributor to mortality[14].

Pregnant and postpartum women in our cohort with LVSD had KCCQ-P values in the range considered 'very poor to poor' and 'poor to fair' highlighting the profound impact of cardiomyopathy associated with LVSD on a woman's quality of life and health throughout gestation and postpartum. Given the challenge in detecting cardiomyopathy with clinical risk factors (especially in isolation), this study also highlights the need to consider digital biomarkers that can be applied at low cost and at scale, such as an

artificial intelligence-enabled electrocardiogram[40] which could potentially augment the performance of the KCCQ-P score.

Key strengths of this study include enrollment of diverse racial and ethnic groups, performance of a symptom assessment and a comprehensive transthoracic echocardiogram on the same day (or within 24 hours) in all patients, as well as the novel use of a validated health assessment questionnaire. The use of a simple questionnaire such as this could be a cost-effective method to improve LVSD screening in general, as well as in low-resource settings. This questionnaire may also be useful in low-middle income countries with high maternal mortality rates, and more specifically in sub-Saharan Africa which accounted for 70% of global maternal deaths in 2020[4]. However, before broad adoption in non-US populations, the cultural and linguistic adaptation of the questionnaire in addition to validation studies in similar patient populations are essential. Screening could allow for better risk stratification and identification of those who would benefit from cardiovascular testing and or referral but the validity of the KCCQ-P in a population with a higher prevalence of cardiomyopathy would require further

study. However, our findings should be interpreted in the context of potential limitations, including a relatively small sample size with a low prevalence of LVSD, no clinical assessment of diastolic heart failure, and GLS is not routinely obtained if echocardiograms are performed during pregnancy or postpartum. Echocardiographic measures such as diastolic function and markers of elevated filling pressures were assessed as these may suggest diastolic heart failure. Women with LVSD had higher estimated left ventricular filling pressures based on E/e' > 15. However, we found no statistically significant differences in KCCQ-P scores when stratified by echocardiographic diastolic function status. In addition, the KCCQ was adapted for pregnancy and although it had good internal consistency and reliably differentiated women with apparent and subclinical LVSD from those with normal LV systolic function, the full psychometric properties of the scale warrant further study.

In this initial evaluation of an adaptation of the KCCQ-12 for pregnant individuals, we found that the KCCQ-P effectively discriminated apparent/subclinical LVSD from normal LV systolic function in an obstetric population. This tool could potentially be used for identifying individuals with a high likelihood of cardiomyopathy with LVSD during the peripartum period who may benefit from additional evaluation including echocardiography. Larger studies are needed to validate this finding, its utility for identifying other forms of cardiomyopathy (including those with preserved left ventricular ejection fraction), an assessment of serial changes in KCCQ-P scores at different timepoints in pregnancy and examine its impact on pregnancy outcomes.

DATA AVAILABILITY

The data underlying this article will be shared on reasonable request to the corresponding author. All requests for raw and analyzed data and related materials will be reviewed by the Mayo Clinic legal department and Mayo Clinic Ventures to verify whether the request is subject to any intellectual property or confidentiality obligations. Requests for patient-related data not included in the paper will not be considered. Any data and materials that can be shared will be released via a Material Transfer Agreement.

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ACKNOWLEDGEMENTS

AUTHOR CONTRIBUTIONS

D.A., H.H. and R.C. had full access to all of the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: D.A., R.C., P.N. and J.P. Acquisition, analysis, or interpretation of data: D.A., A.M., K.Y., Y.B., C.R., D.B., K.S., M.F., S.P., H.H., R.C. and J.P. Drafting of the manuscript: D.A. and A.M. Critical revision of the manuscript for important intellectual content: J.S., K.F., A.M., P.J., K.Y., E.D., Y.B., C.R., D.B., K.S., M.F., S.P., P.N. and R.C. Statistical analysis: H.H., D.A. and R.C. Administrative, technical, or material support: A.M. and E.D. Supervision: P.N., R.C. and J.P.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s44294-024-00005-3.

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