Trends in cardiorespiratory fitness: The evolution of exercise treadmill testing at a single Academic Medical Center from 1970 to 2012

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Objective To identify temporal trends in the use of exercise treadmill testing (ETT) and cardiorespiratory fitness (CRF) estimated by ETT in metabolic equivalents (METs).

Patients and methods We compiled an ETT database of all available treadmill tests—including those with concomitant stress echocardiography and nuclear perfusion imaging studies—performed at Duke University Hospital from January 1, 1970-December 31, 2012. Six different ramp protocols were used in these combined modalities. CRF at maximal exertion was estimated using established metrics. Eligible patients were required to have no missing data on maximal treadmill speed, grade, and protocol.

Results The most commonly used ETT protocol was the Bruce (n = 28,877), followed by manual test (n = 7390). Since the 1980's, the use of ETT for clinical purposes declined substantially; there was a decreased trend in utilization of 9.4% over the decades 1990–1999 and 2000–2009. When standard protocol (Bruce) was assessed in isolation, trends in CRF decreased progressively from 1970 to 2012 (mean METs (standard deviation): 11.7 (4.3) to 10.5 (3.5)). After adjusting for baseline comorbidities, the trend was reduced to a lesser degree.

Conclusions The use of ETT at our institution has declined over time, perhaps due to changes in clinical practice. In patients undergoing ETT using the standard Bruce protocol, CRF decreased progressively over the last five decades. Future studies are needed to clarify the etiology of the decrease in use of such a powerful predictor of clinical outcomes in our medical care environment. (Am Heart J 2019;210:88-97.)

Cardiorespiratory fitness (CRF)—defined as energy expenditure at the peak of a maximal exercise stimulus and measured indirectly with respiratory gas exchange—is the strongest individual predictor of mortality across a broad range of disease states, from cardiovascular disease to cancer.[1-4] In recent years, the utility of fitness in cardiovascular risk prediction in clinical practice has been supplanted by novel imaging modalities and risk prediction algorithms.[5] Such algorithms ignore the predictive power provided by maximal exercise testing and ignore the potential increase in accuracy that might be provided by including them in risk prediction models.

Over the last few decades, cardiovascular mortality related to coronary heart disease has significantly decreased in the United States.[6,7] However, these improvements in mortality are being threatened and potentially attenuated by increasing rates of diabetes and obesity in the setting of low levels of physical activity and consequent cardiorespiratory fitness.[8] The most recent data suggest median lifespan for the first time is slipping in our aging populations. Along with a strong independent, inverse relation with all-cause mortality and cardiovascular disease, CRF is strongly associated with obesity, diabetes and subsequent development of other CV risk factors.[1,2,9-12] In all individuals, CRF decreases over the lifespan; however, as a modifiable risk factor,

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Table I. Exercise testing protocols over time

Treadmill test protocol	All (N = 46,022)	1970–1979 (N = 1615)	1980–1989 (N = 7906)	1990–1999 (N = 18,256)	2000–2009 (N = 16,539)	2010–2012 (N = 1706)
Bruce	28,875/46022 (62.7%)	1615/1615 (100.0%)	6897/7906 (87.2%)	11,030/18256 (60.4%)	8467 (51.2%)	866 (50.8%)
Modified Bruce	1346/46022 (2.9%)	0/1615 (0.0%)	384/7906 (4.9%)	637/18256 (3.5%)	296 (1.8%)	29 (1.7%)
Balke	2054/46022 (4.5%)	0/1615 (0.0%)	369/7906 (4.7%)	1636/18256 (9.0%)	49 (0.3%)	0 (0.0%)
Others	67/46022 (0.1%)	0/1615 (0.0%)	0/7906 (0.0%)	0/18256 (0.0%)	66 (0.4%)	1 (<0.1%)
Manual	7390/46022 (16.1%)	0/1615 (0.0%)	2/7906 (<0.1%)	530/18256 (2.9%)	6165 (37.3%)	693 (40.6%)
Ekelund	6290/46022 (13.7%)	0/1615 (0.0%)	254/7906 (3.2%)	4423/18256 (24.2%)	1496 (9.0%)	117 (6.9%)

improvements in clinical outcomes can be obtained through improvements in fitness through regular physical activity and exercise.[13-15]

Furthermore, from 1950 to 2000—and presumably through the present—the US population has become increasingly sedentary.[16] However, these physical activity data are based on questionnaire data, which are limited by recall bias and survey collection instruments. CRF is closely related to an individual's daily physical activity levels, and can thus be closely estimated with measures obtained during exercise stress testing. To our knowledge, CRF has not been assessed over time in a significantly large at-risk clinical population. Understanding the trends in CRF over time can help patients, clinicians, and researchers understand the unique interplay of CV risk factors, CRF, and clinical outcomes. We sought to evaluate changes in the use of ETT at a single major academic medical center and the associated changes in CRF estimated by ETT over multiple decades.

Methods

Study Population

All available Duke University Medical Center exercise treadmill tests (ETT) from 1970 to 2012 performed at the Duke Center for Living, Cardiac Diagnostic Unit and Nuclear Laboratory were combined into a single database. Included were treadmill exercise tests performed with or without imaging echocardiograms or nuclear perfusion scans at Duke between 1970 and 2012. Patients of age 18 or older with available peak treadmill speed and grade were included (n = 46,022). For patients with multiple stress tests during the study period, only the initial test was analyzed. Only tests performed on a treadmill were considered—bicycle tests were excluded.

Measurements

During the period exercise testing used multiple exercise treadmill protocols: Bruce,[17] modified Bruce,[18] Balke,[19] Ekelund,[20] and other manually controlled protocols. CRF (in METs) was estimated based on the combined information derived from peak treadmill speed and peak percentage treadmill grade attained during testing based on previously used methods.[21] Specifically, if peak treadmill speed was <100 m/min, then CRF = [0.1*(peak treadmill speed in meters/min) + 1.8*(peak treadmill speed in meters/min)*(percent grade peak treadmill incline) +3.5]/3.5. If peak treadmill speed was ≥100 meters/min, then CRF = [0.2*(peak treadmill speed in meters/min) + 0.9*(peak treadmill speed in meters/min)*(percent grade peak treadmill incline) + 3.5]/3.5.

Outcomes of interest

Peak metabolic equivalents (METs) were the units for cardiorespiratory fitness estimates based on a patient's maximal achieved treadmill speed and percent grade.

Statistical analysis

We performed a retrospective analysis of ETT utilization and CRF from 1970–2012. ETT utilization is shown as relative change in total ETT studies performed between decades (1970–1979, 1980–1989, 1990–1999, 2000–2009, and 2010–2012). Baseline characteristics included demographics, vital signs, past medical history, and physical examination results. Baseline characteristics, etiology of ETT termination, and CRF in METs are summarized by decades. The comorbidities of chronic kidney disease, COPD, dialysis, connective tissue disease, and metastatic cancer were not collected with the ETTs prior to 1984, so they are not reported for subjects who had treadmill tests before 1984. Distribution of CRF in METs for each exercise treadmill protocol is presented in a box plot. Categorical variables are summarized as frequencies and percentages, and continuous variables are by means and standard deviations. In order to avoid the risks of confounding by case mix, the analyses of CRF over time was restricted to participants who performed the Bruce Protocol. The trend in CRF from 1970–2012 is presented in a figure where the crude mean METs as well as the adjusted mean METs and its 95% confidence intervals were estimated for each year. Factors included in the adjustment model were: age, gender, history of ischemic heart disease, diabetes mellitus, congested heart failure, myocardial infarction, hypertension, hyperlipidemia, peripheral vascular disease, cerebrovascular disease, and prior tobacco use. Given a large amount of missing information for BMI, it was not included in the adjustment model.

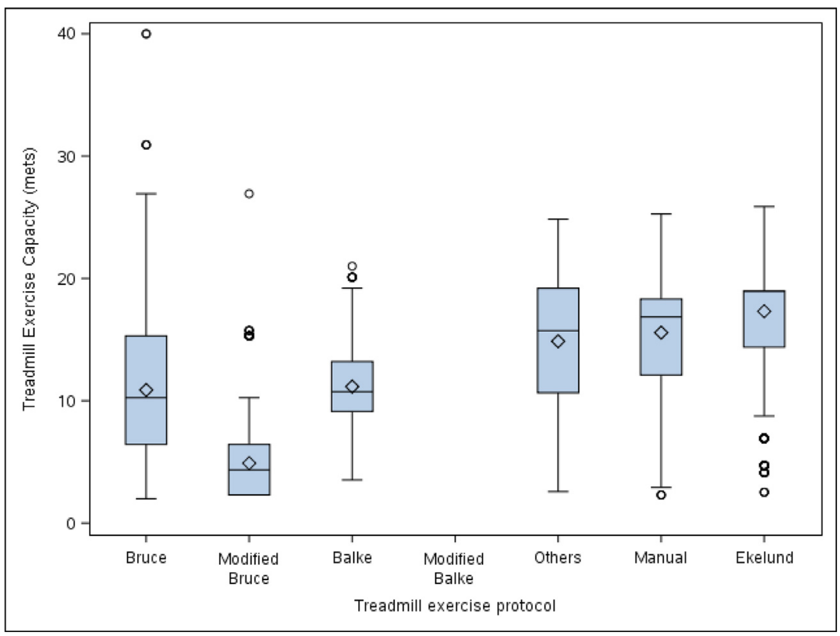
Table II. Baseline characteristics among subjects who performed the Bruce protocol

	All (N = 28,875)	1970–1979 (N = 1615)	1980–1989 (N = 6897)	1990–1999 (N = 11,030)	2000–2009 (N = 8467)	2010–2012 (N = 866)
Demographics						
Age at the test						
N	27,073	1601	6336	10,204	8070	862
Mean (SD)	53.6 (12.2)	48.6 (8.9)	53.2 (11.9)	53.4 (12.8)	54.6 (12.0)	57.5 (11.2)
Female	10,198/28597 (35.7%)	465/1602 (29.0%)	1879/6633 (28.3%)	4001/11029 (36.3%)	3470/8467 (41.0%)	383/866 (44.2%)
Male	18,399/28597 (64.3%)	1137/1602 (71.0%)	4754/6633 (71.7%)	7028/11029 (63.7%)	4997/8467 (59.0%)	483/866 (55.8%)
Caucasian	21,536/28875 (74.6%)	1537/1615 (95.2%)	5681/6897 (82.4%)	7856/11030 (71.2%)	5880/8467 (69.4%)	582/866 (67.2%)
Black	5062/28875 (17.5%)	49/1615 (3.0%)	785/6897 (11.4%)	2138/11030 (19.4%)	1860/8467 (22.0%)	230/866 (26.6%)
Other race	1588/28875 (5.5%)	5/1615 (0.3%)	141/6897 (2.0%)	671/11030 (6.1%)	717/8467 (8.5%)	54/866 (6.2%)
Race unknown	689/28875 (2.4%)	24/1615 (1.5%)	290/6897 (4.2%)	365/11030 (3.3%)	10/8467 (0.1%)	0/866 (0.0%)
Medical history						
History of ischemic heart disease	10,132/28875 (35.1%)	1039/1615 (64.3%)	3176/6897 (46.0%)	3072/11030 (27.9%)	2476/8467 (29.2%)	369/866 (42.6%)
Coronary artery bypass graft surgery	6704/28875 (23.2%)	32/1615 (2.0%)	1423/6897 (20.6%)	2873/11030 (26.0%)	2191/8467 (25.9%)	185/866 (21.4%)
Congestive heart failure	2364/28875 (8.2%)	82/1615 (5.1%)	410/6897 (5.9%)	1118/11030 (10.1%)	656/8467 (7.7%)	98/866 (11.3%)
Chronic kidney disease	326/26212 (1.2%)	Not collected	2/5849 (<0.1%)	73/11030 (0.7%)	186/8467 (2.2%)	65/866 (7.5%)
History of dialysis	25/26212 (<0.1%)	Not collected	0/5849 (0.0%)	9/11030 (<0.1%)	11/8467 (0.1%)	5/866 (0.6%)
History of smoking	8243/28875 (28.5%)	1026/1615 (63.5%)	2575/6897 (37.3%)	2529/11030 (22.9%)	1895/8467 (22.4%)	218/866 (25.2%)
Chronic obstructive pulmonary disease	448/26212 (1.7%)	Not collected	31/5849 (0.5%)	212/11030 (1.9%)	181/8467 (2.1%)	24/866 (2.8%)
Diabetes	3403/28875 (11.8%)	141/1615 (8.7%)	621/6897 (9.0%)	1079/11030 (9.8%)	1329/8467 (15.7%)	233/866 (26.9%)
Hypertension	9808/28875 (34.0%)	549/1615 (34.0%)	2008/6897 (29.1%)	2994/11030 (27.1%)	3643/8467 (43.0%)	614/866 (70.9%)
Hyperlipidemia	6917/28875 (24.0%)	349/1615 (21.6%)	1073/6897 (15.6%)	2196/11030 (19.9%)	2787/8467 (32.9%)	512/866 (59.1%)
Peripheral vascular disease	1061/28875 (3.7%)	62/1615 (3.8%)	313/6897 (4.5%)	391/11030 (3.5%)	252/8467 (3.0%)	43/866 (5.0%)
Cerebrovascular disease	1286/28875 (4.5%)	14/1615 (0.9%)	224/6897 (3.2%)	504/11030 (4.6%)	448/8467 (5.3%)	96/866 (11.1%)
Connective tissue disease	148/26212 (0.6%)	Not collected	21/5849 (0.4%)	49/11030 (0.4%)	71/8467 (0.8%)	7/866 (0.8%)
History of metastatic cancer	327/26212 (1.2%)	Not collected	14/5849 (0.2%)	132/11030 (1.2%)	162/8467 (1.9%)	19/866 (2.2%)
Diagnosis/baseline measures						
Weight in kg						
N	20,562	252	3572	8625	7251	862
Mean (SD)	85.9 (22.2)	81.7 (17.5)	81.1 (16.4)	85.3 (22.7)	88.6 (23.6)	89.7 (22.7)
BMI in kg/m^2						
N	19,994	249	3515	8173	7209	848
Mean (SD)	28.8 (6.6)	27.2 (5.3)	27.0 (4.7)	28.6 (6.6)	29.8 (7.1)	30.2 (6.8)
Baseline heart rate (beats/min)						
N	16,821	0	6617	6954	3114	136
Mean (SD)	78.5 (15.3)		80.2 (14.9)	78.6 (15.3)	75.2 (15.6)	68.3 (13.8)
Baseline systolic blood pressure (mm Hg)						
N	17,235	1042	6032	6988	3051	122
Mean (SD)	133.4 (22.1)	120.4 (19.0)	130.5 (20.8)	135.0 (22.4)	139.8 (22.4)	135.3 (19.1)
Baseline ejection fraction						
N	13,616	1	2275	4123	6371	846
Mean (SD)	54.7 (11.1)	41.0	48.3 (8.2)	51.9 (9.6)	58.0 (11.3)	60.7 (11.5)
Medications						
Beta blocker use prior to treadmill test	7021/28875 (24.3%)	Not collected	342/6897 (5.0%)	2389/11030 (21.7%)	3807/8467 (45.0%)	483/866 (55.8%)

Table II (*continued*)

	All (N = 28,875)	1970–1979 (N = 1615)	1980–1989 (N = 6897)	1990–1999 (N = 11,030)	2000–2009 (N = 8467)	2010–2012 (N = 866)
Health status						
No history of MI or cerebrovascular disease or diabetes or hypertension	15,166/28875 (52.5%)	800/1615 (49.5%)	3357/6897 (48.7%)	6616/11030 (60.0%)	4192/8467 (49.5%)	201/866 (23.2%)

Figure 1



Unadjusted cardiorespiratory fitness (METs) by exercise protocol. Results are graphically displayed in box plot as medians and interquartile ranges (box); upper and lower 25% of data values, excluding outliers (whiskers); means (squares); and outliers (circles).

Results

The ETT protocol types and frequencies are presented in Table I. The most frequently utilized ETT protocols were the Bruce[17] (62.7%), other manual (16.1%) and Ekelund[20] (13.7%). ETT utilization for all protocol types was less by 9.4% when comparing the decade 1990–1999 to 2000–2009. The baseline characteristics of patients referred for Bruce protocol ETT are described in Table II. Of the 28,875 patients referred for Bruce protocol ETT between 1970 and 2012 with complete data, the mean patient age was 48.6 in 1970–1979 and 57.5 in 2010–2012. Percentages of women, black, and other races completing ETT became gradually greater across the decades. Prevalences of ischemic heart disease and smoking history were greatest in the decade 1970–1979 —64.3% and 63.5%—but only 42.6% and 25.2% by the interval 2010–2012. The prevalence of previous coronary artery bypass grafting (CABG) was 26.0% in 1990–1999, but only 21.4% in 2010–2012. However, patients referred for ETT had gradually greater prevalences of congestive heart failure (CHF), diabetes, hypertension and hyperlipidemia for the period beginning 1970 through 2012. The mean weight was 81.7 kg in 1970 but 89.7 kg by 2012. The mean body mass index (BMI) was 27.2 in 1970–1979, but 30.2 by 2010–2012. The baseline systolic blood pressure was 120.4 mmHg in 1970–1979, but 139.8 mmHg by 2000–2009; however, the mean heart rate was 80.2 beats per minute in 1980–1989, but only 68.3 beats per minute by 2010–2012. This reflects the use of beta-blockers before the ETT, which was 5.0% in the

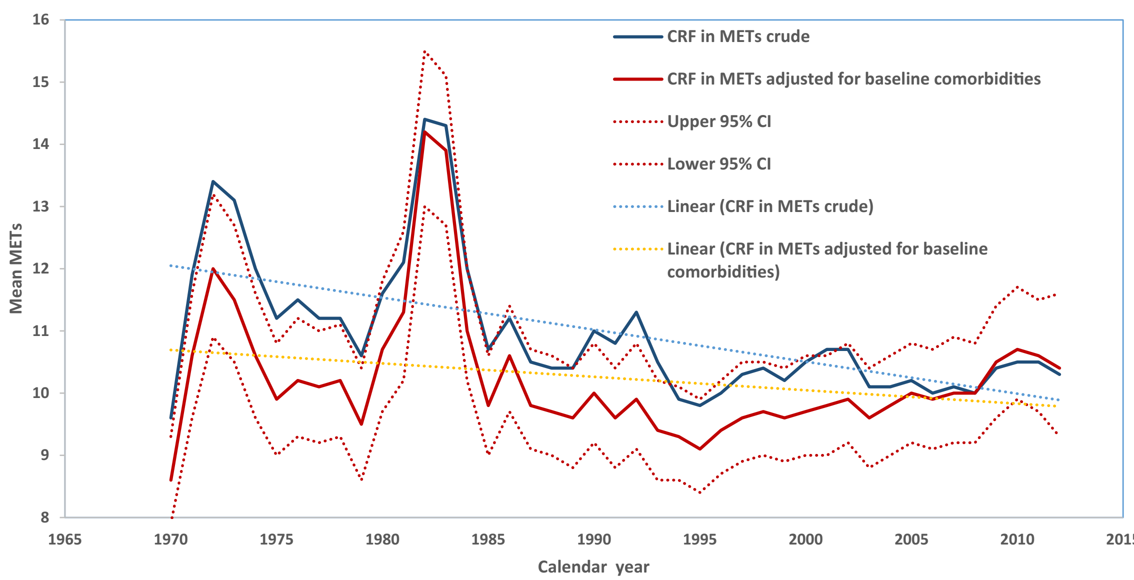
Table III. Trends in CRF by decade and stratified by age and comorbidities among subjects who performed the Bruce protocol

	All (N = 28,875)	1970–1979 (N = 1615)	1980–1989 (N = 6897)	1990–1999 (N = 11,030)	2000–2009 (N = 8467)	2010–2012 (N = 866)
Treadmill exercise capacity in METs (TEC)						
N	28,875	1615	6897	11,030	8467	866
Mean (SD)	10.9 (3.9)	11.7 (4.3)	11.5 (4.0)	10.6 (3.8)	10.6 (3.7)	10.5 (3.5)
Duke Treadmill Score						
N	25,569	637	5369	10,431	8288	844
Mean (SD)	5.8 (5.3)	–0.1 (7.7)	7.5 (4.4)	5.6 (5.4)	5.5 (5.1)	5.5 (4.9)
Subgroup analyses of TEC in METs						
Age <20						
N	123	0	32	69	22	N/a
Mean (SD)	14.2 (3.4)	N/a	13.6 (4.1)	14.1 (3.4)	15.2 (2.4)	N/a
20 < = age < = 29						
N	604	31	167	262	134	10
Mean (SD)	13.7 (3.7)	14.4 (4.8)	14.5 (3.1)	13.5 (3.8)	13.2 (3.7)	10.6 (3.1)
30 < = age < = 39						
N	2533	224	602	1042	632	33
Mean (SD)	12.4 (3.9)	12.9 (4.4)	13.5 (3.9)	12.2 (3.8)	11.6 (3.7)	12.6 (3.8)
40 < = age < = 49						
N	6767	594	1493	2571	1942	167
Mean (SD)	11.6 (3.8)	11.9 (4.4)	12.4 (3.8)	11.2 (3.7)	11.4 (3.7)	11.2 (3.5)
50 < = age < = 59						
N	8296	569	2020	2867	2573	267
Mean (SD)	10.6 (3.7)	11.3 (4.1)	11.1 (3.8)	10.2 (3.6)	10.6 (3.6)	10.7 (3.4)
60 < = age < = 69						
N	6053	172	1535	2239	1842	265
Mean (SD)	9.4 (3.3)	10.2 (3.6)	9.8 (3.4)	9.0 (3.2)	9.5 (3.3)	10.2 (3.3)
70 < = age < = 79						
N	2419	11	450	1046	810	102
Mean (SD)	8.3 (2.7)	8.6 (2.9)	8.5 (2.8)	8.2 (2.6)	8.2 (2.6)	9.2 (3.4)
Age > = 80						
N	278	N/a	37	108	115	18
Mean (SD)	7.8 (2.5)	N/a	9.9 (4.3)	7.3 (1.6)	7.4 (2.2)	8.3 (2.0)
Female						
N	10,198	465	1879	4001	3470	383
Mean (SD)	9.5 (3.4)	11.5 (3.9)	9.8 (3.5)	9.3 (3.4)	9.3 (3.3)	9.3 (3.0)
Male						
N	18,399	1137	4754	7028	4997	483
Mean (SD)	11.6 (3.9)	11.8 (4.4)	12.0 (3.9)	11.3 (3.9)	11.5 (3.8)	11.5 (3.5)
White						
N	21,536	1537	5681	7856	5880	582
Mean (SD)	11.0 (3.9)	11.7 (4.3)	11.4 (3.9)	10.7 (3.8)	10.8 (3.8)	10.7 (3.6)
Black						
N	5062	49	785	2138	1860	230
Mean (SD)	10.0 (3.7)	11.4 (4.5)	10.9 (3.9)	9.9 (3.7)	9.7 (3.5)	9.8 (3.1)
Other race						
N	1588	5	141	671	717	54
Mean (SD)	11.3 (3.8)	13.6 (5.3)	11.6 (3.9)	11.3 (3.8)	11.3 (3.7)	11.3 (3.1)
Diabetes – No						
N	25,472	1474	6276	9951	7138	633
Mean (SD)	11.1 (3.9)	11.7 (4.3)	11.7 (4.0)	10.8 (3.8)	10.9 (3.8)	10.9 (3.6)
Diabetes – Yes						
N	3403	141	621	1079	1329	233
Mean (SD)	8.9 (3.1)	11.1 (3.9)	9.6 (3.6)	8.3 (2.7)	8.8 (3.0)	9.4 (3.0)
Smoking – No						
N	20,632	589	4322	8501	6572	648
Mean (SD)	11.2 (3.9)	11.8 (4.2)	12.0 (4.1)	11.0 (3.9)	10.9 (3.8)	10.8 (3.5)
Smoking – Yes						
N	8243	1026	2575	2529	1895	218
Mean (SD)	10.1 (3.7)	11.6 (4.3)	10.8 (3.9)	9.2 (3.2)	9.4 (3.2)	9.8 (3.2)
With a history of MI/ cerebrovascular disease/ diabetes/hypertension						

Table III (*continued*)

	All (N = 28,875)	1970–1979 (N = 1615)	1980–1989 (N = 6897)	1990–1999 (N = 11,030)	2000–2009 (N = 8467)	2010–2012 (N = 866)
N	15,387	1316	3958	4811	4613	689
Mean (SD)	9.8 (3.6)	11.3 (4.1)	10.6 (3.8)	9.1 (3.3)	9.5 (3.3)	10.2 (3.4)
No history of MI/ cerebrovascular disease /diabetes/hypertension						
N	13,488	299	2939	6219	3854	177
Mean (SD)	11.8 (3.9)	12.0 (4.4)	12.6 (4.0)	11.5 (3.8)	11.7 (3.8)	11.6 (3.5)

Figure 2



Trends in cardiorespiratory fitness (in METs) over time using the Bruce protocol. Results are graphically displayed 1) unadjusted, 2) adjusted for age, gender, history of ischemic heart disease, diabetes mellitus, congested heart failure, myocardial infarction, hypertension, hyperlipidemia, peripheral vascular disease, cerebrovascular disease, and prior tobacco use.

decade1980–1989, but 55.8% by 2010–2012. Baseline ejection fraction, as calculated by echocardiography or nuclear perfusion scan, was 48.3 in 1980–1989, but 60.7 in 2010–2012. The health status defined as no history of myocardial infarction, cerebrovascular disease, diabetes, or hypertension was greatest—60.0%—in 1990–1999, but only 23.2% in 2010–2012.

CRF distributions in METs for each exercise treadmill protocol are presented in Figure 1. Trends in CRF for patients who performed the Bruce protocol only are characterized in Table III. The mean CRF (standard deviation) was 11.7 (4.3) METs in 1970–1979, but only 10.5 (3.5) METs in 2010–2012. The mean Duke Treadmill Score was −0.1 in 1970–1979; but greater—5.5—in 2010–2012. The mean CRF in 10-year age groups from 1970–2012 was gradually less over the age decades of 20–29, 30–39, 40–49, 50–59, and 80 or older; however CRF was relatively constant in age decade 60–69 and greater in age groups <20 and 70–79 over the study interval. Patients of white or black race, female gender, past medical history of diabetes, smoking, or a health status of MI/cerebrovascular disease/diabetes/hypertension had less CRF over the intervals 1970–1979 to 2010–2012. Patients of male gender or a health status of no MI/cerebrovascular disease/diabetes/hypertension had relatively stable CRF over the intervals 1970–1979 to 2010–2012. Figure 2 displays the unadjusted and adjusted trends in CRF of patients who completed the Bruce protocol.

Reasons for ETT termination for patients completing the Bruce protocol are summarized by decade in Table IV. From 1970 to 1979, the most common reasons for termination were chest discomfort (64.1%) and arrhythmia (19.9%). Chest discomfort, arrhythmia, and ST changes became less

Table IV. Trends in etiology of ETT termination among subjects who performed the Bruce protocol

	All (N = 28,787)	1970–1979 (N = 1606)	1980–1989 (N = 6891)	1990–1999 (N = 10,998)	2000–2009 (N = 8424)	2010–2012 (N = 866)
Reason for termination						
Musculoskeletal	11 (<0.1%)	0 (0.0%)	0 (0.0%)	7 (<0.1%)	4 (<0.1%)	0 (0.0%)
Other hemodynamic	193 (0.7%)	0 (0.0%)	24 (0.3%)	118 (1.1%)	50 (0.6%)	1 (0.1%)
Other	761 (2.6%)	0 (0.0%)	265 (3.8%)	273 (2.5%)	210 (2.5%)	13 (1.5%)
Max heart rate reached	699 (2.4%)	17 (1.1%)	139 (2.0%)	304 (2.8%)	222 (2.6%)	17 (2.0%)
Chest discomfort	2441 (8.5%)	1030 (64.1%)	344 (5.0%)	497 (4.5%)	508 (6.0%)	62 (7.2%)
Claudication	210 (0.7%)	0 (0.0%)	126 (1.8%)	52 (0.5%)	30 (0.4%)	2 (0.2%)
Fatigue	14,946 (51.9%)	0 (0.0%)	4484 (65.1%)	6119 (55.6%)	3980 (47.2%)	363 (41.9%)
Dyspnea	6737 (23.4%)	102 (6.4%)	854 (12.4%)	2659 (24.2%)	2807 (33.3%)	315 (36.4%)
Planned	133 (0.5%)	0 (0.0%)	33 (0.5%)	45 (0.4%)	43 (0.5%)	12 (1.4%)
ST changes	1011 (3.5%)	137 (8.5%)	484 (7.0%)	309 (2.8%)	66 (0.8%)	15 (1.7%)
Arrhythmias	490 (1.7%)	320 (19.9%)	105 (1.5%)	49 (0.4%)	13 (0.2%)	1 (0.1%)

common in subsequent decades. Fatigue accounted for 65.1% of reasons for ETT termination from 1980–1989, but decreased in frequency over time to 41.9% in 2010–2012. Dyspnea became a more common etiology of ETT termination, increasing from 6.4% from 1970–1979 to 36.4% from 2010–2012.

Discussion

To test for trends in ETT usage and CRF over time, we used a clinical database of patients referred for ETT at a single academic medical center spanning four-plus decades (1970–2012). When evaluating the most commonly used Bruce protocol, mean CRF was less by 1.2 METs (11.7 to 10.5 METs) over these four-plus decades of observation. Also, during this same period the population presented for evaluation with progressively more CV risk factors—presence of diabetes, hypertension, dyslipidemia, and obesity. Despite caring for an enriched population of patients with characteristics associated with worse cardiovascular outcomes, the trend in ETT utilization in these patients to obtain CRF was less by 9.4% over the periods 1990–1999 to 2000–2009. At the same absolute fitness capacity (CRF), increases in body mass result in less relative CRF, as measured by exercise time in this study. Thus, the less fitness capacity over the later study periods compared with the earlier ones may reflect the greater body masses over time. However, future studies are needed to clarify the inverse relationship of increasing BMI and comorbidity burden with decreasing CRF over time in patient populations such as the one studied in this report.

ETT utilization at Duke University increased throughout the 1990s, with peak utilization of ETT in the early 2000s. In patients who can exercise, an ambulatory ETT is a class I recommendation over pharmacologic stress testing (IIa recommendation).[22] The additive predictive value above and beyond pharmacologically-induced abnormalities traditionally placed ETT (with or without imaging) as the preferred method at most stress testing laboratories.[23] For example, testing exercise capacity using exercise testing with or without gas exchange unmasks gender differences in the relationship of fitness to cardiovascular risk: even though men only achieve 1.7 greater METs on average, women have the same predicted mortality as men with 2.6 greater MET capacity.[24] Despite guideline-supported recommendations and the added clinical value of measuring exercise capacity (CRF), our ETT laboratory experience and that of other institutions appear to be moving towards less use of ETT.[25] This trend may eventually lead to adverse clinical outcomes when less predictive, more costly tools are relied upon in place of ETT. More studies are needed to clarify the reasons behind the trend in decreased utilization of ETT in modern clinical settings.

The increased utilization of other non-invasive stress imaging studies may have led to the decreased ETT utilization over the four decades of our study. In the 1990's and 2000's pharmacologic imaging studies became more commonly used, especially in populations with perceived exercise limitations. Given that musculoskeletal conditions may preclude the use of ETT in favor of pharmacologic interventions, the increasing incidence of obesity and associated lower extremity osteoarthritis may be one explanation for decreased ETT usage.[25,26] Further, cardiac MRI with pharmacologic stress has gained popularity for evaluation of patients with breathlessness or heart failure. Although we have maintained significant interest in determining CRF through cardiopulmonary exercise testing at Duke to care for our large local and referral advanced heart failure population to predict candidacy, survival and timing of cardiac transplantation and mechanical circulatory support, this is a relatively small clinical population overall.[27,28]

Hypertension, diabetes and dyslipidemia increased in prevalence in our ETT-referral population over each subsequent decade. The percentage of women referred to ETT increased from 29.0% in 1970–1979 to 44.2% in 2010–2012, likely reflecting changes in epidemiology and increased recognition of CVD occurrence in women.[29] The mean patient age was greater by 8.9 years (48.6 to 57.5) 1970–1979 to 2010–2012. The mean age of 53.6 is similar to that of the Henry Ford Exercise Testing Project (mean age 54 ± 10 years), a clinical cohort spanning the years 1991–2009.[30] It is interesting that we observed an increased in the prevalence of diabetes corresponding to decrease in fitness over time. This is consistent with the observation of Chow et al in the Coronary Artery Risk Development in Young Adults (CARDIA) study: even when adjusting for BMI, greater fitness in young adults was associated with a less risk for developing incident pre-diabetes or diabetes 20 years later.[31] Consistent with recent US data from NHANES demonstrating that 35% of men and 40.4% of women were obese in 2013–2014,[32] we observed an increased prevalence of overweight and obesity over time. As noted, the decreased functional capacity over time may simply reflect the increase in body mass and mean age in the population. That being said, a decrease in cardiorespiratory fitness in a large cardiovascular referral population should be a major cause for concern.

CRF is expected to decrease approximately 1% a year or approximately 10% per decade of life.[8] However, CRF for a given population adjusted for age should be stable. Patients referred for the Bruce protocol in our clinical diagnostic laboratory did, in fact, present with less fitness (11.7 versus 10.5 METs) over the study period. Similar to the experience of the Henry Ford Exercise Testing Project (median MET level 10),[30] the individuals at Duke undergoing testing with the Bruce protocol demonstrated the expected age-related decline in CRF. This trend in reduced CRF over time is alarming given the strength of association with mortality as well as the benefits of risk stratification and reclassification of patients with intermediate CVD risk in both the short-term and long-term beyond risk estimates from traditional risk factors.[33] A single measurement of low fitness in mid-life is associated with greater risk of cardiovascular disease—especially among individuals with a high burden of CVD risk factors, such as studied here.[15]

Reduced fitness suggests a population now exists with greater risk for adverse cardiovascular events; this may be due in part to the growing prevalence of physical inactivity and sedentary behavior—which is, itself, a complex interplay of cultural and socio-economic issues.[16] Our simultaneous findings of increasing comorbidities of diabetes, hypertension and dyslipidemia along with increased BMI, obesity and less fitness characterize a population that is becoming unwell while it is simultaneously becoming less fit. It is challenging to decipher the cause-and-effect relationships, but the trends are clear. Although not specifically measured, less fitness suggests reduced physical activity in the study—and perhaps general—population.

Reasons for ETT termination also changed over time. Chest discomfort, EKG changes, and fatigue became less common etiologies over the decades, while dyspnea became more common. The differences in clinical factors leading ETT termination over time may reflect changes in referral patterns for ETT, with more patients with suspected coronary artery disease being referred straight to angiography or other imaging test modality as previously discussed. These findings may also represent changes in the clinical characteristics of patients referred, with more obesity and associated metabolic co-morbidities. Further evaluation of how ETT outcomes are influenced by prescribing patterns and patient characteristics merits further study and may guide understanding as to why ETT utilization and fitness have decreased over time.

The findings of our analysis should be considered in light of a few key limitations. This was a retrospective analysis without randomization using clinical data collected from multiple ETT laboratory locations. ETT without direct measures of gas exchange provides only an estimate of CRF; the lack of simultaneous gas exchange data does not provide an objective estimate of whether a patient has reached a maximal or peak exercise steady state—true maximal effort. Clinical exercise tests may be stopped early due to a clinical endpoint (e.g., angina) or a predetermined diagnostic endpoint (e.g., reaching 95% or greater of age predicted maximum heart rate); this may lead to an underestimate of the true fitness of the individual. This was a single-center study combining ETT from imaging and non-imaging stress tests; thus, there is a potential for referral and selection bias for the type of ETT (bicycle versus treadmill) or non-ETT functional study—using pharmaceutical rather than exercise stress test—such as used in stress MRI. These potential biases may limit the generalizability of our observations to other institutions that may have different utilization rates and referral for ETT. There is a potential for bias related to unknown and unmeasured underlying health status across multiple decades of patients. Our observations were robust to adjustments for age and health status; however, despite adjustment, other measured and unmeasured covariables may have influenced these results. Notably, we did not adjust for weight, BMI, race, or medications given the high percentage of missing data in these categories. As noted, there may also have been bias related to changes in referral patterns over time for ETT including use of stress MRI and cardiopulmonary exercise testing. Despite these potential limitations, the provocative inverse relationship of increasing comorbidities, weight and BMI and decreasing use and level of CRF in patients undergoing Bruce protocol-based ETT suggests that this interaction should be further studied.

Conclusions

The trend in use of ETT has declined over time, perhaps due to changes in clinical practice. In patients undergoing

ETT using our standard Bruce protocol, CRF was progressively less over the last five decades; simultaneously, the prevalence of comorbid conditions, BMI and weight were greater in our referral populations during the same time period. Our findings highlight the value of measuring CRF despite the apparent decreased utilization of ETT, which is a worrisome trend that may lead to worse clinical outcomes. Future studies are needed to clarify the inverse relationship of increasing BMI and comorbidity burden with decreasing CRF, and the etiology of the decrease in use of such a powerful predictor of clinical outcomes in our medical care environment.

Disclosures

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