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Original Contribution

Variation in diagnostic testing for older patients with syncope in the emergency department

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ABSTRACT

Background: Older adults presenting with syncope often undergo intensive diagnostic testing with unclear benefit. We determined the variation, frequency, yield, and costs of tests obtained to evaluate older persons with syncope.

Methods: We conducted a prospective, multicenter observational cohort study in 11 academic emergency departments in the United States of 3686 patients aged ≥60 years presenting with syncope or presyncope. We measured the frequency, variation, yield, and costs (based on Medicare payment tables) of diagnostic tests performed at the index visit.

Results: While most study rates were similar across sites, some were notably discordant (e.g., carotid ultrasound: mean 9.5%, range 1.1% to 49.3%). The most frequently-obtained diagnostic tests were initial troponin (88.6%), chest x-ray (75.1%), head CT (42.5%) and echocardiogram (35.5%). The yield or proportion of abnormal findings by diagnostic test ranged from 1.9% (electrocardiogram) to 42.0% (coronary angiography). Among the most common tests, echocardiogram had the highest proportion of abnormal results at 22.1%. Echocardiogram was an outlier in total cost at $672,648, and had a cost per abnormal test of $3129.

Conclusion: Variation in diagnostic testing in older patients presenting with syncope exists. The yield and cost per abnormal result for common tests obtained to evaluate syncope are also highly variable. Selecting tests based on history and examination while also prioritizing less resource intensive and higher yield tests may ensure a more informed and cost-effective approach to evaluating older patients with syncope.

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1. Introduction

Syncope is the transient loss of consciousness followed by spontaneous and complete recovery. Syncope accounts for 740,000 emergency department (ED) visits and 250,000 hospital admissions in the United States (US), with an estimated annual cost of $2.5 billion annually [1]. Differentiation between life-threatening etiologies such as arrhythmias and benign etiologies such as vasovagal syncope is often difficult during an ED evaluation. This clinical dilemma is particularly pertinent to older adults (≥60 years) who have more co-morbidities and a higher incidence of adverse outcomes. Seven percent of older adults with undifferentiated etiology of syncope in the ED experience death or serious cardiac outcome within 30 days [2].

These factors contribute to wide variability in diagnostic testing. For example, rates of hospital based testing have been previously shown to range between 39 and 78% for echocardiogram, and 6–19% for cardiac stress test [3-9]. Prior investigators have explored the frequency and attempted to determine the value of diagnostic tests performed in the ED for older patients presenting with syncope [10, 11]. However, the generalizability of these findings has been limited by exclusion of discharged patients, retrospective design, single-center experience, and unclear reliability of judgments about the clinical value of testing. Furthermore, since the publication of these prior studies, there have been important US health policy changes influencing the diagnostic approach to patients with syncope. The Medicare Recovery Audit Contractor (RAC) program launched nationwide to retrospectively identify "unnecessary" hospital admissions in 2010, and Diagnosis Related Group 312: Syncope & Collapse has been a top target for this initiative [12]. Providers have been pressured to avoid inpatient care in this patient population, and practice patterns may have changed because of the RAC program.

Using a prospective, multi-center study design that included all patients ≥60 years old presenting to the ED with syncope or near-syncope, we describe the inter-hospital variation, frequency, yield, and costs for common diagnostic tests ordered in the evaluation of syncope. We hypothesized wide site-level variation in testing rates, with low yield in high-prevalence diagnostics and high total costs associated with such testing.

2. Methods

2.1. Design and setting

We conducted a multicenter prospective cohort study at 11 geographically distributed academic EDs in the US between 2013 and 2016 (see online appendix Table e-1). All patients underwent an independent standardized history, physical examination, and electrocardiogram (ECG) testing by study protocol (see online appendix Fig. e-1). Any additional diagnostic testing was performed at the discretion of the treating providers, and availability of diagnostic testing was similar across sites. Trained research assistants screened for eligible patients using standard definitions, approached candidates, and collected data variables consistent with reporting guidelines for ED-based syncope research and patients' directly reported symptoms [13].

We abstracted objective quantitative data, such as laboratory test results, from the electronic medical record. We performed chart reviews and called patients 30-days after the index ED visit. Study staff obtained outside hospital records if the patient had a visit to a facility different from the index ED visit. Trained abstractors recorded data on diagnostic testing, including reports of abnormal findings.

The Institutional Review Boards at all enrolling sites approved our study and study staff obtained written informed consent from all participating subjects or their legally authorized representatives. The National Heart, Lung, and Blood Institute funded this study. The sponsors had no influence on study design, access to data, or influence on reporting of results.

2.2. Participants

We enrolled consecutive patients ≥60 years with syncope or near-syncope who presented or were still present in the ED during hours of study staff coverage. We defined near-syncope as sensation of imminent syncope without loss of consciousness. We included patients with traumatic injuries that occurred as a result of syncope or near-syncope. We excluded patients with a presumptive cause of loss of consciousness due to seizure, stroke or transient ischemic attack, or hypoglycemia. We also excluded patients who were intoxicated from alcohol or other drugs, patients requiring medical or electrical intervention to restore consciousness, and patients who were unable or unwilling to provide informed consent or follow-up information.

2.3. Outcome measures

Our primary outcomes were the prevalence of diagnostic testing and proportion of abnormal tests at the index visit, which included ED care as well as subsequent observation or inpatient care, if needed. We chose significant abnormal findings according to the most recently available national specialty society guidelines or authoritative peer-reviewed publications, whenever available (see online appendix Table e-2). For example, we classified neuroimaging with angiogram as "abnormal" for acute aneurysm rupture or any ≥70% or "severe" intracranial artery occlusion in symptomatic patients in the study interpretation according to published guidelines [14]. Some tests required additional interpretation. For example, we defined an elevated troponin result as "abnormal" only if elevated ≥3× the "normal" cutoff for the site-specific assay plus a final diagnosis of myocardial infarction at the index ED visit.

In contrast to prior investigations, we chose not to infer whether an abnormal test finding was causative or "diagnostic" for the patient's presenting symptom of syncope or presyncope [3-5, 7]. Our data collection forms did require local research staff to indicate whether a test was diagnostic based on chart review. However, in our preliminary analysis we found unacceptably low inter-rater reliability around this determination. Many charts simply had insufficient data to make a reliable judgment. Therefore, as described previously we used an objective list of criteria based on literature review.

Two physician abstractors independently reviewed all abnormal results to group them into major abnormal findings. All abstractors were second or third year emergency medicine residents who reviewed a training set of at least 10 reports for each diagnostic study in conjunction with two of the study investigators (CWB, BCS). Investigators adjudicated any discrepancies in categorization to reach unanimous agreement prior to data analysis.

Our secondary outcomes were costs associated with diagnostic tests. We estimated the total costs of each diagnostic test by using 2017 national unadjusted Medicare payment tables to proxy both facility and professional costs [15, 16]. Prior work by our group validated a Medicare payment approach against actual costs from hospital accounting data [17].

2.4. Data analysis

We reported yields as percentages. Denominators were the number of tests obtained, and the numerators were the number of tests in which findings were abnormal. We estimated total costs associated with each test by multiplying the number of tests obtained and the estimated unit cost per test. We determined cost per abnormal test by dividing the total costs by the number of abnormal tests. We generated dot plots to illustrate site-level variation in test ordering. We used the REDcap system to manage study data and performed statistical analyses using SAS (SAS version 9.4; SAS Institute Inc., Cary, NC) and the R package [18, 19].

3. Results

3.1. Characteristics of participants

We enrolled 3686 patients and completed 30-day follow up on 3676 after 10 patients withdrew from the study, as shown in the online appendix Fig. e-2. We illustrate the characteristics of study subjects in Table 1. Mean age was 72.7 years and the cohort was 48.5% female. Hypertension was the most common comorbidity at 66.1% and 22.3% of patients reported a prior history of arrhythmia. Just over a quarter (25.1%) of patients had a serious outcome diagnosed at the index visit or within the 30-day follow up window, led by arrhythmia at 8.4%. Only 0.9% of patients had a diagnosis of pulmonary embolus.

Table 1
Characteristics of study patients ($N = 3686$).

Characteristic	No. (%, SD)
Age, mean (SD)	72.7 (9.0)
Female	1786 (48.5)
History	
Hypertension	2436 (66.1)
Previous episode of syncope	1317 (35.7)
Coronary artery disease	1017 (27.6)
Diabetes mellitus	904 (24.5)
Arrhythmia	823 (22.3)
Ventricular arrhythmia/sudden death	38 (1.0)
SVT (includes PAT, PSVT, atrial fibrillation, atrial flutter)	511 (13.9)
Sick sinus syndrome, Mobitz II, complete heart block, junctional rhythm	61 (1.7)
Congestive heart failure	469 (12.7)
Previous stroke	464 (12.6)
Dementia	281 (7.6)
Symptoms preceding syncopal episode	
Light-headedness	1991 (54.0)
Chest pain	325 (8.8)
Mental status change	563 (15.3)
Symptoms suggestive of stroke	57 (1.5)
Physical examination findings	
Presence of cardiac murmur	356 (9.7)
Neurological deficits on examination	208 (5.6)
Initial disposition following ED visit	
Discharge home	738 (20.0)
Place in observation	1394 (37.8)
Admit to inpatient	1462 (39.7)
AMA/eloped	36 (1.0)
Died	8 (0.2)
Other	411 (11.2)
Serious 30-day outcomes[a]	
Arrhythmia	308 (8.4)
Myocardial infarction	70 (1.9)
Cardiac intervention[b]	159 (4.3)
Pulmonary embolism	35 (0.9)
NEW diagnosis of structural heart disease	35 (0.9)
Stroke (both ischemic and hemorrhagic)	29 (0.8)
Aortic dissection	0 (0)
Subarachnoid hemorrhage (spontaneous)	2 (0.1)
Cardiopulmonary resuscitation	8 (0.2)
Internal hemorrhage/anemia requiring transfusion	169 (4.6)
Recurrent syncope/fall resulting in major traumatic injury	12 (0.3)
Recurrent syncope, after index hospital visit	99 (2.7)

[a] $N = 3676$ (excludes withdrawals at 30-day phone follow-up.)
[b] e.g., pacemaker or internal cardiac defibrillator placement, percutaneous coronary intervention, coronary artery bypass grafting.

3.2. Primary outcomes

Fig. 1 shows the variation in frequency of testing across the 11 study sites. While most study rates were similar across sites, some were notably discordant. Carotid ultrasound had the widest range (mean 9.5%, minimum 1.1% and maximum 49.3%), followed by head CT (mean 42.9%, minimum 26.2% and maximum 65.9%), echocardiogram (mean 35.5%, minimum 18.9% and maximum 56.5%), chest x-ray (mean 75.1%, minimum 52.2% and maximum 86.6%) and initial troponin (mean 88.6%, minimum 76.7% and maximum 98.6%). We list the specific mean, minimum and maximum rates of occurrence across the sites for each diagnostic test in the online appendix Table e-3.

We display the overall incidence and proportion of abnormal findings of diagnostic tests in Table 2. The most frequently-obtained diagnostic tests were ECG (100%, mandated by the study protocol), initial troponin (88.6%), chest x-ray (75.1%), head CT (42.5%) and echocardiogram (35.5%). The proportion of abnormal findings on diagnostic testing ranged from 1.9% (ECG) to 42.0% (coronary angiography). Among the top five most common tests, echocardiogram had the highest proportion of abnormal results at 22.1%.

We list the total costs and cost per abnormal study for each diagnostic test in Table 3. Echocardiograms accounted for the highest total costs at $672,648, with a cost per abnormal test at $3129. On a cost per abnormal test basis, electrophysiology (EP) study was significantly higher than all others, at $39,703. Only 1.2% of patients had this testing performed, but a modest proportion of abnormal studies (13.6%) combined with the highest cost per study ($5414) created this outlier in cost per abnormal study. Holter monitoring resulted in a relatively low cost per abnormal result of $817.

Finally, in Fig. 2, we illustrate the test frequency versus cost per test. In this graph, an inverse relationship is more clearly demonstrated, showing high-cost tests such as EP study, cardiac catheterization and endoscopy were performed at much lower frequencies. Echocardiogram and CT head are revealed as a moderate cost tests with relatively high frequency. In addition, studies most frequently performed (e.g., ECG, chest x-ray, initial troponin) were the lowest-cost tests.

4. Discussion

The diagnostic evaluation of near syncope and syncope in older patients presenting to the ED varies widely. Of concern is the extent to which unhelpful, and presumably unnecessary, testing in the evaluation of syncope continues to be performed despite decades of compelling evidence. For example, nearly half of patients underwent a head CT (42.9%) and results were abnormal in only 3.6%, resulting in relatively high cost per abnormal result ($4341) compared with other tests we studied. These costs do not factor in other potential harms of CT scanning, such as the risk of ionizing radiation and the additional length of stay added to an ED visit. In addition, the high cost per abnormal test for EP testing is aligned with the most recent specialty society recommendations, which classifies this test as Class III (no benefit) in patients with a normal ECG and no structural heart disease [20, 21]. The continued use of non-evidence-based diagnostics and variability among sites reveals that many clinicians are uncertain of how best to evaluate this patient population.

Our approach of reporting on objective abnormal findings rather than “diagnostic” findings results in a higher yield than previously reported in studies on this topic [3-5, 7]. The subjective nature of retrospectively determining a test is “diagnostic” via a medical record vulnerable to incomplete data, variability of test result reports and lack of validation or assessment of inter-rater reliability create challenges in interpreting these prior papers. Our approach of double-abstractor review is a major methodologic advance but does create a conservative bias. As a result, tests appear more useful than they actually are in this population because the truly valuable “diagnostic” results, which we can't measure, are a subset of the “abnormal” results

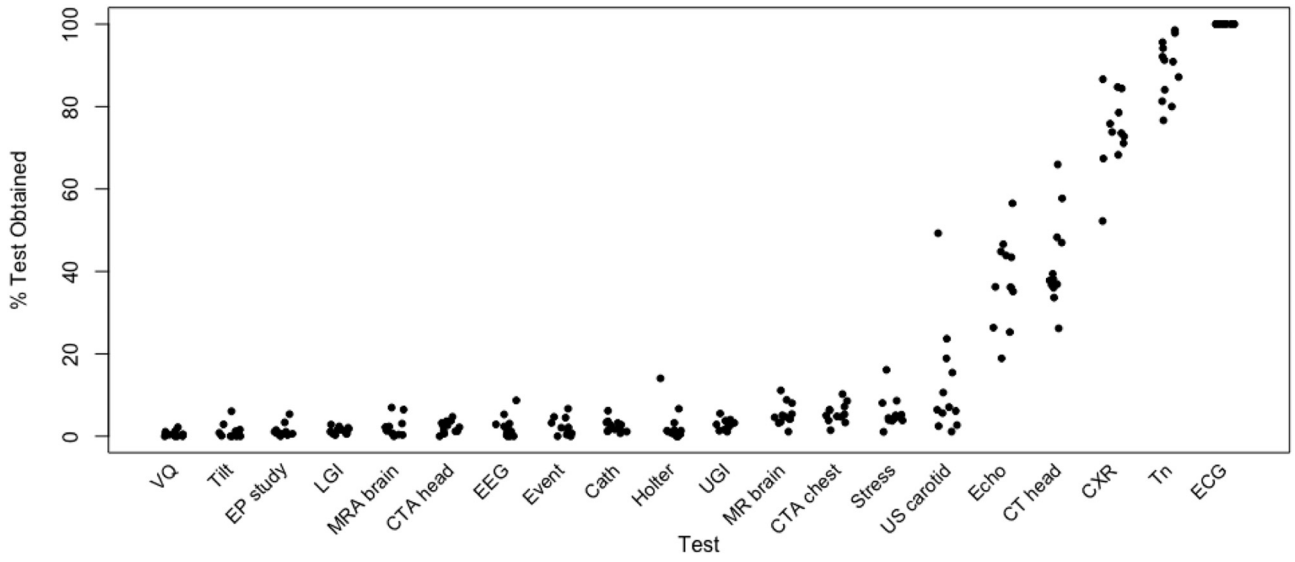

Fig. 1. Variation in test frequency by site Legend: VQ = ventilation perfusion scan, Tilt = tilt table test, EP study = Electrophysiology study, LGI = lower gastrointestinal endoscopy, MRA brain = magnetic resonance angiogram of the brain, CTA head = computed tomography angiogram of the head, EEG = electroencephalogram, Event = event monitor, Cath = cardiac catheterization, Holter = Holter monitor, UGI = upper gastrointestinal endoscopy, MR brain = magnetic resonance imaging of the brain, CTA chest = computed tomography angiogram of the chest, Stress = cardiac stress test, US carotid = Ultrasound of the carotid, Echo = trans-thoracic echocardiogram, CT head = computed tomography of the head, CXR = chest x-ray, Tn = conventional troponin assay, ECG = electrocardiogram.

that we do measure. That is, our estimates can be used as the most optimistic boundary of the value of various tests. In addition, the yields we report lead to generally lower cost per abnormal test compared to previously reported cost per diagnostic test [3].

Our study addresses several other important limitations in previous attempts to estimate the proportion and cost per test of abnormal results in this study population. For example, we enrolled a significantly higher number of subjects than previous investigations in a multicenter design with prospective data collection. We included all patients regardless of disposition. In addition, we used a validated Medicare payment model as a proxy for facility and professional costs. Our results suggest how clinicians might be more selective when obtaining tests to evaluate patients presenting to the ED with syncope, as the wide range in yield of abnormal results and cost per abnormal test we report reveals opportunities to more selectively choose a diagnostic workup. Prior studies also used single site cost-to-charge ratios to estimate costs [3]. Our Medicare payment-based method is more valid, less prone to bias and more generalizable across institutions and regions [3, 17].

The data reflecting variation in testing across study sites reveal that some testing is nearly ubiquitous in the study population, such as initial troponin and chest x-ray. This may be explained by the relatively low barriers to obtaining and interpreting these tests versus others, as they are rapidly obtained 24/7, pose minimal risk to the patient and are easily interpreted directly by an emergency physician. However, these tests also were among the lowest yield for abnormal results in our study, which suggests indiscriminate ordering in patients with no other clinical indication other than their complaint of syncope or pre-syncope,

Table 2
Frequency and diagnostic yield of tests obtained in evaluation of syncopal episodes in older patients.

Test[a]	Obtained		Abnormal	
	N	(%)	N	(%)
Electrocardiogram[b]	3686	100	69	1.9
Troponin	3265	88.6	41	1.3
Chest x-ray	2767	75.1	182	6.6
Head CT	1581	42.9	57	3.6
Echocardiogram	1307	35.5	289	22.1
Carotid ultrasound	350	9.5	44	12.6
Chest CT angiogram	214	5.8	32	15.0
Brain MRI	194	5.3	21	10.8
Cardiac stress test	180	4.9	21	11.7
Holter monitor	177	4.8	30	16.9
Upper GI endoscopy	110	3.0	36	32.7
Head CT angiogram	97	2.6	17	17.5
Coronary angiography	88	2.4	37	42.0
Electroencephalogram	81	2.2	2	2.5
Event monitor	73	2.0	14	19.2
Brain MRI angiogram	71	1.9	4	5.6
Lower GI endoscopy	53	1.4	11	20.8
Electrophysiology study	44	1.2	6	13.6
Tilt table test	32	0.9	10	31.3
VQ scan	17	0.5	5	29.4

[a] We excluded the following tests due to low incidence ($N < 20$) except for VQ scan: carotid massage, implantable loop recorder, ambulatory blood pressure monitoring on discharge and transcranial ultrasound.
[b] Initial ECG on presentation to the ED.

Table 3
Costs of abnormal diagnostic tests in the evaluation of syncopal episodes.

Test	Cost per test, $[a]	Total cost, $	Cost per abnormal test, $
Electrocardiogram	63.16	232,807.76	3374.03
Troponin[c]	13.50	44,077.50	1075.06
Chest x-ray	70.99	196,429.33	1079.28
Head CT	156.83	247,948.23	4349.97
Echocardiogram	514.65	672,647.55	3128.59
Carotid ultrasound	267.01	93,453.50	2123.94
Chest CT angiogram	358.53	76,725.42	2397.67
Brain MRI	376.28	72,998.32	3476.11
Cardiac stress test[b]	856.93	220,231.74	10,487.23
Holter monitor	138.42	24,500.34	816.68
Upper GI endoscopy	1546.93	170,162.30	4726.73
Head CT angiogram	354.94	34,429.18	2025.25
Coronary angiography	3085.13	271,491.44	7337.61
Electroencephalogram	291.17	23,584.77	11,792.39
Event monitor	783.45	57,191.85	4085.13
Brain MRI angiogram	287.64	20,422.44	5105.61
Lower GI endoscopy	862.90	45,733.70	4157.61
Electrophysiology study	5414.10	238,220.40	39,703.40
Tilt table test	512.05	16,385.60	1638.56
VQ scan	483.42	8218.14	1643.63

[a] Costs include facility and professional components, expressed in 2017 US dollars.
[b] Weighted average cost of exercise tolerance test, stress echo and nuclear perfusion stress tests.
[c] Includes patients with a diagnosis of myocardial infarction at index ED visit.

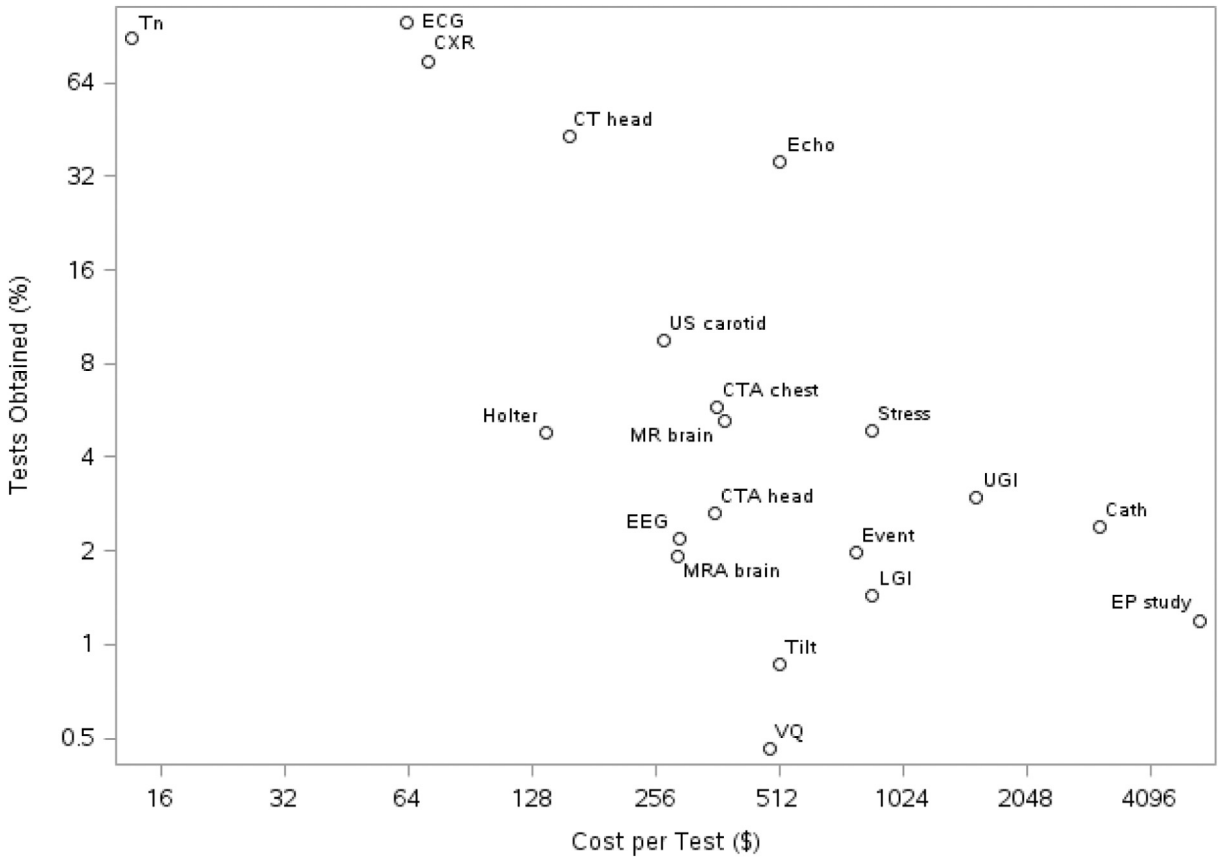

Fig. 2. Test frequency versus cost per test (log scale) Legend: VQ = ventilation perfusion scan, Tilt = tilt table test, EP study = Electrophysiology study, LGI = lower gastrointestinal endoscopy, MRA brain = magnetic resonance angiogram of the brain, CTA head = computed tomography angiogram of the head, EEG = electroencephalogram, Event = event monitor, Cath = cardiac catheterization, Holter = Holter monitor, UGI = upper gastrointestinal endoscopy, MR brain = magnetic resonance imaging of the brain, CTA chest = computed tomography angiogram of the chest, Stress = cardiac stress test, US carotid = Ultrasound of the carotid, Echo = trans-thoracic echocardiogram, CT head = computed tomography of the head, CXR = chest x-ray, Tn = conventional troponin assay, ECG = electrocardiogram.

especially for initial troponin and chest x-ray, should be pursued with caution. Chest x-ray is not discussed as a diagnostic modality by professional society syncope guidelines, exhibited an abnormal rate of only 6.6% in our study, and may create downstream costs for incidental findings [20]. Conversely, higher rates of abnormal testing in infrequent modalities with significant barriers to obtain them or higher patient risk (i.e., coronary angiography, with a yield of 42%) likely reflect more careful patient selection with high pretest probability. As a result, it would be erroneous to conclude that such tests should be performed for every older patient presenting to the ED with syncope or near syncope.

Echocardiography is another test that was frequently obtained (35.5% of subjects), with a higher yield (22.1%) likely due to more selective testing, but the total cost of this test was an outlier at $672,648. This disproportionate cost emphasizes the importance of using evidence-based patient selection criteria to identify those patients most likely to benefit [20, 22]. In addition, while only 9.5% of study subjects underwent a carotid ultrasound, it was the most variable test we studied and had a relatively low yield (12.6%). Attributing abnormal carotid ultrasound results as a causative explanation for the presentation of syncope is especially problematic, as unilateral carotid stenosis is unlikely to result in syncope [23, 24]. While carotid vessel imaging may have been accomplished via alternative testing (i.e., CT angiogram, MR angiogram) in sites with low use of carotid ultrasound, routine carotid imaging is not considered standard of care in the study population [20].

We found an incidence of 0.9% of pulmonary embolism at 30 days, consistent with other recent investigations [25]. This result differs significantly from 17.3% recently reported by Prandoni et al. in another study [26]. This difference may be explained by different study populations, as their analysis only included hospitalized patients and we studied a much larger US-based cohort. Our findings suggest pulmonary embolism is a rare but present diagnosis in the study population. As a result, pulmonary embolism should be entertained in the differential diagnosis and pursued only in patients with a history, exam and risk factors suggestive of it as a causative diagnosis.

Our findings may inform value-based clinical metrics to encourage more rational testing. Several national campaigns are underway for this purpose (e.g., Choosing Wisely) and reducing unnecessary and costly diagnostic testing is a topic of great interest to both payers and increasingly, hospitals, as the trend towards bundled payments and Accountable Care Organizations continues [27]. Looking ahead, one can expect an increased emphasis on the stewardship of costly, low-yield diagnostics. In addition, Medicare's RAC program has previously focused on short-stay hospitalizations for syncope as a major source of reclaimed payments. Providers choosing to hospitalize patients for "further diagnostic testing" should consider safe and feasible alternatives, such as a focused observation unit evaluation or expedited outpatient clinic follow up.

Syncope and pre-syncope are a common symptom of numerous clinical conditions. As a result, a clinically-useful, sensitive risk stratification tool to inform diagnostic testing has been elusive. The San Francisco Syncope Rule failed to hold up in subsequent validation studies [28, 29]. Future research in this area is needed to help clinicians tailor the diagnostic workup and disposition destination, especially in older patients where the concern for more dangerous diagnoses is higher.

5. Limitations

Our results should be interpreted with several limitations. We did not include an analysis of orthostatic vital signs in our analysis, which

have previously been touted as a test with low cost and high diagnostic yield [3]. Orthostatic vital signs have proven to be a controversial topic in the role of syncope evaluation, as there is a high-degree of subjectivity in interpreting results and assigning as a causative mechanism for the presenting episode, especially since patient-reported symptoms are typically included as a "positive" result [30-34]. While the cost to perform this test is comprised only of the staff time to perform and interpret them, we chose not to include them in our analysis due to the lack of objectivity in their interpretation. We also do not estimate downstream costs – such as unnecessary subsequent testing and/or hospitalization – from false-positive test results, which are more likely to occur in patients with low pre-test probability [35-37].

We also chose not to include certain common diagnostic tests in our analysis, such as telemetry, venous labs aside from initial troponin and serial ECG. We noted discrepancies in data capture and missing data for these non-billable procedures that made the analysis too inconsistent to report. Finally, we did not consider whether the abnormal finding was already known, was a newly discovered abnormal finding (e.g., depressed ejection fraction).

6. Conclusion

In this large, multi-center, prospective study using more accurate cost estimates than prior analyses and inclusion of all patients regardless of disposition, we found the proportion and costs of abnormal results in common tests obtained to evaluate syncope to be highly variable. Selecting tests based on history and examination and prioritizing less resource intensive and higher yield tests may ensure a more informed and cost-effective approach to evaluating older patients presenting to the ED with pre-syncope and syncope. Future research is needed to develop evidence-based diagnostic guidelines, which may lessen the extent of unnecessary testing. Basing testing on the results of the initial history and examination and prioritizing higher yield tests would ensure a more informed and cost-effective approach to evaluating this population.

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Conflicts of interest

CWB has received advisory board and speaker's fees from Roche Diagnostics, research funding from Janssen Pharmaceuticals and Boehringer Ingelheim, and consulting and advisory board fees from Janssen Pharmaceuticals. DHA has received research funding from Roche Diagnostics. AB has received research funding from Radiometer and Portola. AB has been a consultant for Portola. JMC has received funding from Astra Zeneca. CLC has received research funding from Radiometer, Ortho Clinical Trials, Janssen, Pfizer, NIH, Portola, Biocryst, Glaxo Smith Klein, Hospital Quality Foundation, and Abbott. She is a consultant for Portola, Janssen, and the Hospital Quality Foundation. DBD is a consultant for Janssen and Roche, has received institutional research support from Novartis, Ortho Scientific, and Roche, and is on the editorial board for Academic Emergency Medicine and Circulation. JEH has received research funding from Alere, Siemens, Roche Diagnostics, Portola, and Trinity. DKN has received honorarium from Pfizer. ABS is a consultant for Siemens and Quidel and is on the Data and Safety Monitoring Board for Trevena. BCS has received consulting fees from Medtronic. All other authors have no conflicts to disclose.

Authorship contributions

CWB and BCS conceived the study and CWB served as lead author. BCS guided the study's design and execution. BWB, BAN, MNS, DHA, AB, JMC, CLC, DBD, JEH, DKN, KA, ABS, STW, and BCS were responsible for data acquisition. ES performed the statistical analysis under the supervision of REW. CWB drafted the manuscript, and all authors contributed substantially to its revision. CWB, REW, ES and BCS designed the statistical analysis CWB takes responsibility for the paper as a whole.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajem.2018.07.043.

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