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THE PRESENT AND FUTURE

JACC STATE-OF-THE-ART REVIEW

Care Models for Acute Chest Pain That Improve Outcomes and Efficiency

JACC State-of-the-Art Review

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ABSTRACT

Existing assessment pathways for acute chest pain are often resource-intensive, prolonged, and expensive. In this review, the authors describe existing chest pain pathways and current issues at the patient and system level, and provide an overview of recent advances in chest pain research that could inform improved outcomes for both patients and health systems. There are multiple avenues to improve existing models of chest pain care, including novel risk stratification pathways incorporating highly sensitive point-of-care troponin assays; new devices available before first medical contact that could allow clinicians to access vital signs and electrocardiogram data; artificial intelligence and precision medicine tools that may guide indications for further testing; and strategies to improve hospital benchmarking and performance monitoring to standardize care. Improving the speed and accuracy of chest pain diagnosis and management should be a priority for researchers and is likely to translate to substantive benefits for patients and health systems.
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Acute chest pain is common and can be caused by a broad range of conditions ranging from benign to life-threatening. To exclude serious and life-threatening conditions, such as acute coronary syndromes (ACS), emergency department (ED) and hospital assessment is frequently required and can be resource-intensive, prolonged, and expensive. Although discussion commonly focusses on improving disease-based outcomes, recent chest pain guidelines have highlighted the importance of monitoring and improving symptom-based care, which provides a more comprehensive representation of health care provision at the patient level.[1] In this review, we aimed to: 1) describe existing chest pain pathways and current problems at a patient and system level, such as hospital overcrowding, high costs, and overtesting; and 2) provide an overview of recent advances in chest pain research that could result in improved acute chest pain assessment models and outcomes for both patients and health systems.

ACUTE CHEST PAIN EPIDEMIOLOGY AND OUTCOMES

Acute chest pain accounts for approximately 5%-10% of attendances to EDs and 10% of calls for assistance to emergency medical services (EMS), with >7 million presentations to ED annually in the United States.[2-4]

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ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndromes

CDP = clinical decision pathway

CMR = cardiac magnetic resonance imaging

CPU = chest pain unit

CT = computed tomography

CTCA = computed tomography coronary angiography

ECG = electrocardiogram

ED = emergency department

EMS = emergency medical services

MACE = major adverse cardiac events

MI = myocardial infarction

ncRNA = noncoding RNA

STEMI = ST-segment elevation myocardial infarction

HIGHLIGHTS

- Acute chest pain is the most common reason for emergency medical contact, but existing assessment pathways for acute chest pain are resource intensive, lengthy, and expensive.
- Advances in point-of-care troponin assays, wearable devices, shared decision-making, noninvasive imaging strategies, artificial intelligence, and big data applications promise to improve management of patients with chest pain.
- Further development and application of these tools could reduce the system burden of chest pain assessment and improve clinical outcomes.

Demand for EMS services for chest pain is growing faster than overall EMS demand and population growth,[5] and lifetime prevalence of acute chest pain has been estimated at 20%-40%.[6] Rates of acute chest pain presentations are marginally higher among women than men.[2] A significant socioeconomic gradient has been described in some studies, with higher incidences of acute chest pain attendances observed among socially disadvantaged cohorts.[7,8] Racial and ethnic differences have been observed, including a higher incidence of acute chest pain among Black and Hispanic patients in the United States.[9-11]

The underlying causes of acute chest pain are broad, and after assessment, one-half of all patients are eventually discharged with a diagnosis of nonspecific pain.[3,4] Nonetheless, life-threatening or serious causes are present in a significant proportion of presentations (**Figure 1**).[12] Although differences are observed across different cohorts and populations, around 25% have a cardiovascular diagnosis, whereas 20%-25% have a noncardiovascular diagnosis.[4] Most common cardiovascular diagnoses include acute coronary syndromes (10%), congestive heart failure (5%), and arrhythmias (5%). Noncardiovascular diagnoses include pneumonia or exacerbations of chronic obstructive pulmonary disease (10%) and gastrointestinal disorders, especially gastroesophagitis (5%). Pulmonary emboli (1%) and acute aortic pathologies (0.3%) are rare but are important conditions to exclude due to high mortality rates.[3]

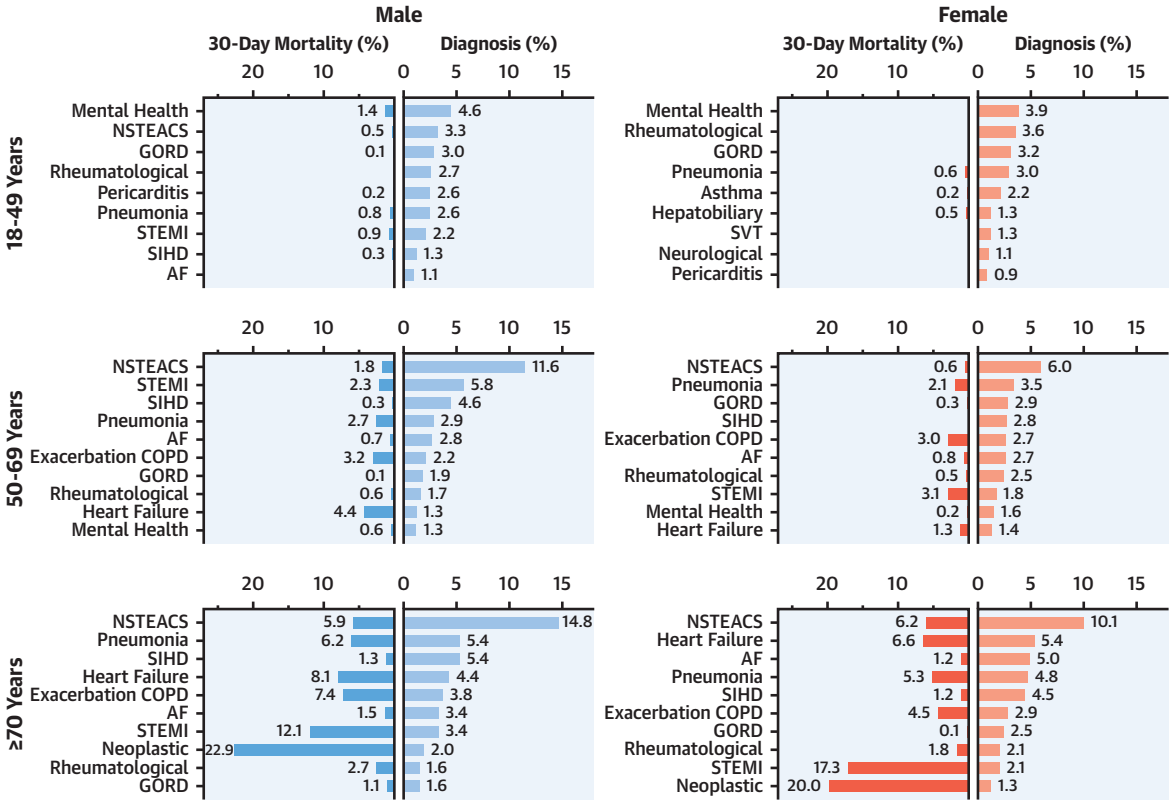
Patient outcomes are dependent on the underlying cause and can vary from mortality rates of <1% for nonspecific pain, to 20% for acute aortic pathologies (**Figure 1**).[12] Overall mortality rates for acute chest pain presentations are approximately 1%-2%, with substantial variation according to patient demographics.[4,12] For patients discharged with an index admission diagnosis of nonspecific chest pain, readmission for serious cardiovascular events including ACS is approximately 3% within 6 months.[13] One-year mortality among patients diagnosed with nonspecific pain is similar to that of the general population.[14,15]

EXISTING MODELS OF ACUTE CHEST PAIN CARE

To avoid missing serious or life-threatening causes of acute chest pain, current guidelines recommend patients or bystanders contact EMS for rapid transfer to the nearest ED for further assessment.[1] Although rapid transfer to hospital remains the priority, the role of EMS has expanded in recent years to include more complex assessment such as 12-lead electrocardiograms (ECGs) and prenotification in ST-segment elevation myocardial infarction (STEMI). Initial ED assessment involves a focused history and examination, combined with targeted investigations that usually include an ECG and troponin sampling, using a stepwise approach aimed at excluding the most serious conditions first. Much of this process is focused on identifying the risk of ACS, with high-risk patients usually admitted and frequently investigated with coronary angiography, whereas intermediate-risk patients are typically investigated with functional or noninvasive anatomical testing, and low-risk patients triaged to no testing or optional testing strategy for coronary artery disease.[1] Existing tools demonstrating improved clinical or system outcomes in assessment and management of acute chest pain are summarized in the following section.

PREHOSPITAL CARE. Thirty percent to 60% of chest pain patients present via ambulance, and several interventions in recent decades have generated improvements in prehospital care for acute chest pain.[16,17] Prehospital ECGs are associated with reduced mortality in undifferentiated chest pain cohorts,[18] possibly through early diagnosis of STEMI, with hospital prenotification and often earlier cardiac catheterization laboratory activation.[19-21] Contacting EMS directly is associated with improved door-to-balloon-times for STEMI,[22] and public health campaigns aimed at educating the community to contact EMS when acute chest pain occurs have similarly been successful in improving public engagement with

FIGURE 1 **Diagnoses and Mortality Among Acute Chest Pain Cohorts**

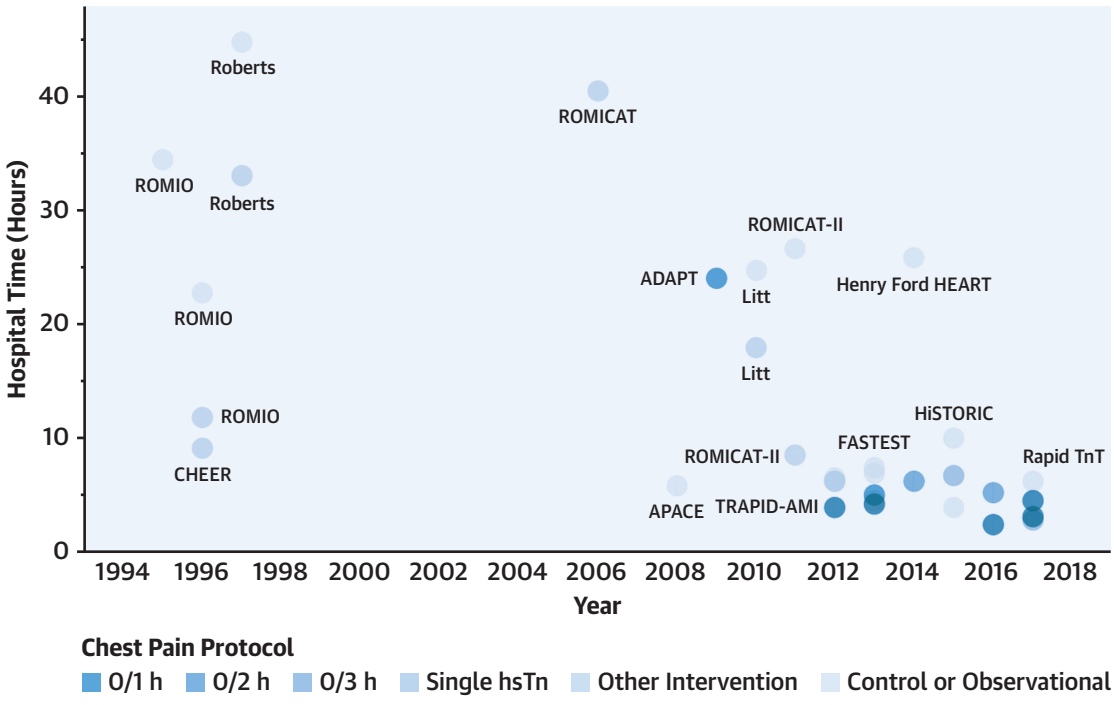


Most common specific diagnoses and 30-day mortality rates among acute chest pain attendances by emergency medical services according to age and sex. Nonspecific pain according to male and female sex accounts for 52.1% and 50.0% in the 18-49-year age group, 47.2% and 53.8% in the 50-69-year age group, and 37.1% and 41.6% in the ≥70-year age group. Internal data from Ambulance Victoria, 2015 to 2019.[12] AF = atrial fibrillation; COPD = chronic obstructive pulmonary disease; GORD = gastroesophageal reflux disease; NSTEACS = non-ST-segment elevation acute coronary syndromes; SIHD = stable ischemia heart disease; STEMI = ST-segment elevation myocardial infarction; SVT = supraventricular tachycardia.

EMS in some jurisdictions.[23] Despite these improvements, uptake of prehospital ECGs can still be improved, with rates approximately 70% among chest pain cohorts.[18] Similarly, delays in ambulance offload times to overcrowded EDs can be improved. These delays have been associated with worsened clinical outcomes and have been a concern in the United Kingdom, the United States, Canada, and Australia.[24,25]

TROPONIN PROTOCOLS. Contemporary troponin assays were developed in the 1990s and substantially improved diagnosis of myocardial infarction (MI) for patients presenting with acute chest pain. However, contemporary cardiac troponin assays were limited by low sensitivity for MI at initial presentation, requiring prolonged periods of testing over 6-12 hours, delaying diagnosis among patients with MI, and delaying discharge among patients without MI (**Figure 2**).[26-28] Advancements in assay technology led to the development of highly sensitive cardiac troponin assays, allowing shorter periods of testing between serial troponin samplings.[29] Coupled with greater understanding regarding the incremental information provided by serial troponin results if troponin assays are within the normal range,[30] recent studies have demonstrated the safety of 3-hour,[31] 2-hour,[32] and subsequently, 1-hour rapid troponin pathways,[32-34] leading to improvements in hospital assessment times (**Figure 3**).[35-37] However, implementation of guideline-recommended rapid troponin pathways is not universal in clinical practice, and hospital admission times can be variable even with institution of such testing protocols, with a median ED length of stay of 2.5 to 4.6 hours among low-risk patients in the 0/1-hour arm of recent trials.[37-39]

FIGURE 2 Temporal Trends in Hospital Assessment Times for Acute Chest Pain

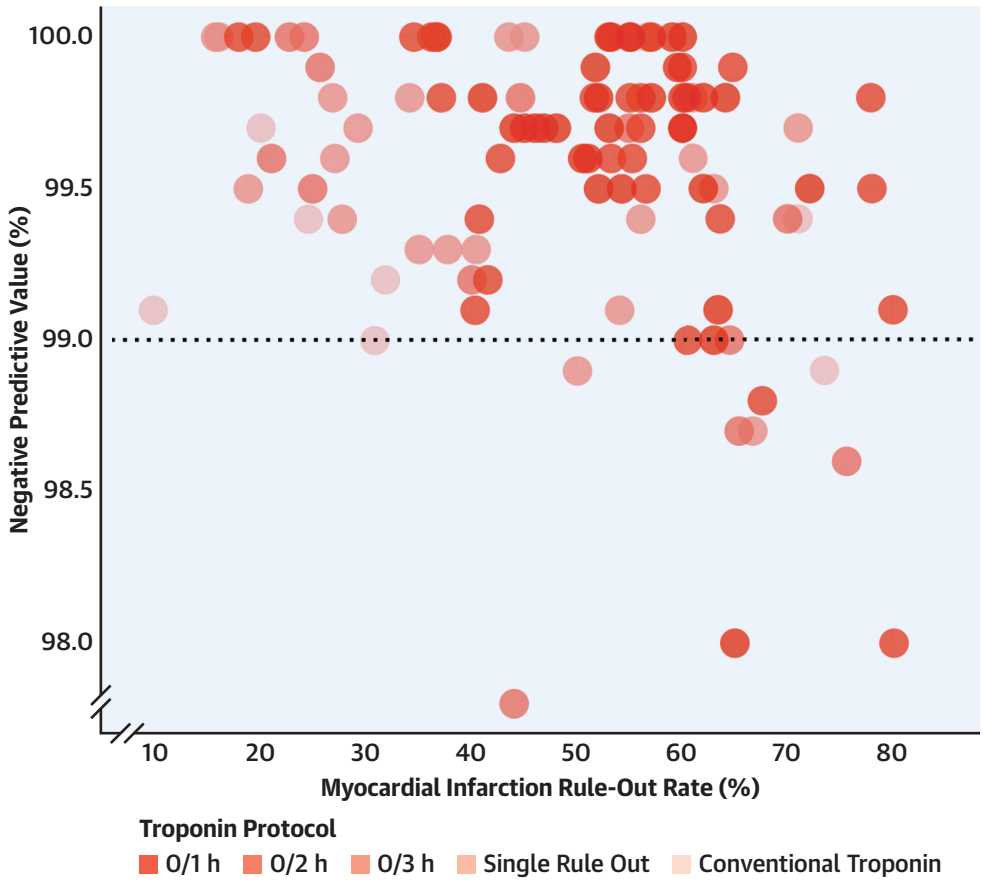


Progression in hospital assessment times for acute chest pain presentations over the last 2 decades in major randomized clinical trials and observational studies. Year of study recruitment is shown on the x-axis in comparison to median hospital assessment times for acute chest pain presentations. Hospital times represent those for patients classified as low-risk of index acute coronary syndrome following initial assessment. Each **point** represents a study with colors representing the protocol used for that patient cohort (legend). Further data regarding these studies are detailed in Supplemental Table I. ADAPT = 2-Hour Accelerated Diagnostic Protocol to Assess Patients With Chest Pain Symptoms Using Contemporary Troponins as the Only Biomarker; APACE = Advantageous Predictors of Acute Coronary Syndrome Evaluation; CHEER = Chest Pain Evaluation in the Emergency Room; FASTEST = Fast Assessment of Thoracic Pain in the Emergency Department Using High-Sensitive Troponins and a Simple Risk Score; Henry Ford HEART = Henry Ford History, ECG, Age, Risk factors, and initial Troponin; HiSTORIC = High-Sensitivity Cardiac Troponin on Presentation to Rule Out Myocardial Infarction; hsTn = highly sensitive troponin; ROMICAT = Rule Out Myocardial Infarction using Computer Assisted Tomography; ROMICAT-II = Rule Out Myocardial Infarction using Computer Assisted Tomography II; ROMIO = The Rapid Rule-Out of Myocardial Ischemia Observation; TRAPID-AMI = The High Sensitivity Cardiac Troponin T Assay for Rapid Rule-out of Acute Myocardial Infarction.

EXISTING RISK STRATIFICATION TOOLS AND CLINICAL DECISION PATHWAYS. Existing risk stratification tools were developed before the availability of highly sensitive troponin assays, with the most common scores including the HEART (History, ECG, Age, Risk factors, and initial Troponin) score, EDACS (Emergency Department Assessment of Chest Pain Score) score, and TIMI (Thrombolysis In Myocardial Infarction) score. In combination with contemporary troponin assays, multiple studies have demonstrated improved sensitivity in detecting 30-day major adverse cardiac events (MACE), and therefore, these tools are recommended when highly sensitive troponin assays are not available.[1] Although these scores have also been validated in the highly sensitive troponin era, their benefit over protocols that use highly sensitive troponin assays alone is less clear, with several studies demonstrating no incremental value in diagnostic classification when such risk scores are added to highly sensitive troponin protocols.[40,41]

Protocolization of ED assessment for patients with acute chest pain through the use of Clinical Decision Pathways (CDPs) have been shown to reduce ED length of stay and rates of unnecessary testing in several studies. Many CDPs are based on risk stratification tools, whereas others, such as the 2020 European Society of Cardiology (ESC) guidelines, use highly sensitive troponin testing alone. The aim of most of these pathways is to classify patients into low-, intermediate-, and high-risk groups, with low-risk groups indicating a risk of ACS within 30 days of ≤1%.[1,30] Several CDPs, including the standard

FIGURE 3 Rule-Out Rates and NPVs in Contemporary Troponin Protocols



Each **shaded circle** represents a cohort of patients undergoing a troponin protocol for acute chest pain (see legend) with comparison between the negative predictive value (NPV, y-axis) and the proportion of patients that have myocardial infarction ruled-out following the test protocol (x-axis). The **dotted reference line** at an NPV of 99.0% indicates the minimum acceptable target NPV for troponin protocols. Data underlying this figure are shown in Supplemental Table II.

and modified HEART pathways,[42,43] the ADAPT (2-Hour Accelerated Diagnostic Protocol to Assess Patients With Chest Pain Symptoms Using Contemporary Troponins as the Only Biomarker) pathway,[36] and the EDACS-ADP pathway[44] have demonstrated consistent reductions of 20%-45% in the need for admission in patients presenting with suspected ACS. These pathways are intended for use once alternate serious diagnoses, such as pneumonia, decompensated heart failure, acute aortic pathologies, and pulmonary emboli, have been excluded.

CHEST PAIN UNITS AND CLINICS. Chest pain units (CPUs) and emergency short stay units have been used to streamline assessment and management of patients with acute chest pain while awaiting serial troponin testing and risk stratification.[45] Germany has been especially proactive in the development and accreditation of a CPU network, which now covers almost the entire country with 336 certified CPUs, including a CPU registry to facilitate quality assurance and research.[46,47] Guidelines for the setup and management of CPUs have been published by the Acute Cardiovascular Care Association and the German Society of Cardiology detailing the organizational structure, physical requirements, technical requirements, and management of patients within the CPU.[45,47] Multiple studies performed during the contemporary troponin assay era, including randomized trials, demonstrated that CPUs improved clinical outcomes, reduced admission rates and costs, and improved patient satisfaction.[48-50] Some CPUs incorporate functional testing such as stress echocardiography, which has been shown to be highly feasible,[51] but available data have not demonstrated

improvements in rates of postdischarge 30-day MACE, in patients undergoing noninvasive testing in CPUs before discharge.[52] Moreover, some studies have identified CPU overuse of functional testing in patients with very low pretest probability.[53] German CPU networks has generally recommended and used separate units within the ED with predefined continuously available beds for chest pain patients.[45,54] In other jurisdictions, the organizational and physical CPU structures have been more varied but often incorporate CPU assessment processes into the main ED without defined beds as long as technical facilities including cardiac monitoring are available. In the United States and some other countries, American College of Cardiology chest pain accreditation and certification is widely used, which is focused on quality improvement and performance monitoring rather than specific CPU organizational structures.[54,55] Rapid troponin testing protocols have reduced rates of admission to CPUs,[56,57] and in this setting, locating CPUs within the ED department may make more logistic sense for centers without established separate CPUs. Similarly, CPU location within the ED may expedite further evaluations if a noncardiac diagnosis is present. Rapid-access chest pain clinics can be an alternative or complementary service for further diagnostic workup and the facilitation of noninvasive testing for appropriate patients at low to intermediate risk of future coronary events, and are associated with earlier diagnosis, reduced unplanned ED reattendances within 30 days of discharge, and reduced overall costs.[58,59] Following ED assessment, postdischarge follow-up with a cardiologist is associated with improved outcomes at 1 year.[60]

CHEST PAIN EVALUATION IN THE COVID-19 ERA

The COVID-19 pandemic has led to substantial challenges in chest pain management requiring consideration of a broader set of differential diagnoses and modifications at each stage of standard chest pain care processes.[61] Acute COVID-19 infection can present with symptoms of chest pain, often of a pleuritic or inflammatory characteristics, which can persist for months following the acute infection—with a prevalence of 22% at 2 months after presentation in 1 study.[62] Acute myocarditis, defined as cardiac symptoms with raised highly sensitive troponin and abnormal ECG, cardiac magnetic resonance imaging (CMR), echocardiogram, or histopathology, is a well-described complication of COVID-19.[61] Rates of COVID-19-related myocarditis vary widely according to definitions, but occur in 0.5%-7.0% of patients based on CMR and autopsy studies.[63,64] Rates of myocarditis complicated by shock are estimated to be higher than that of non-COVID-19 viral myocarditis.[65] Similarly, thromboembolic complications, specifically pulmonary emboli, can occur and may present with chest pain. Patients with cardiovascular symptoms and COVID-19 should undergo comprehensive evaluation with ECG, highly sensitive troponin, and transthoracic echocardiogram testing, and with CMR recommended if initial testing is abnormal.[61] Ischemic testing should be performed in accordance with existing chest pain clinical guidelines.[1]

The subsequent development of COVID-19 vaccines has similarly resulted in concerns regarding postvaccine chest pain presentations, especially regarding risks of myocarditis following mRNA-based vaccinations. Post-mRNA vaccine myocarditis incidence varies according to age and sex, with an estimated incidence of 41 per million vaccinations among males aged <30 years and 4 per million vaccinations among females aged <30 years.[66] The prognosis from vaccine-related myocarditis is generally very good with >95% having a mild clinical course. Nonspecific chest pain and generalized musculoskeletal symptoms without biomarker or imaging evidence of myopericarditis is significantly more common following COVID-19 vaccination.[67]

CHALLENGES AND MODIFICATIONS TO CHEST PAIN MANAGEMENT DURING COVID-19. At the prehospital level, COVID-19 has resulted in reduced ambulance availability, saturation of emergency call lines leading to delays in dispatch, and reduced system efficiencies.[68] Substantial adaptations to infection control measures, including paramedic personal protective equipment, transfer processes to EDs, decontamination of ambulances, and the segregation of hospital resources, all contribute to lost efficiency.[69] At the peak of the pandemic, most jurisdictions instituted full personal protective equipment and N95 masks for paramedics for all attendances, resulting in increased complexity of patient retrieval, delays to EMS response times,[70] and greater difficulties with standard chest pain assessment processes such as prehospital ECGs. Delays to first-ECG, diagnosis, and door-to-balloon times were observed in several studies of patients with STEMI.[71] Screening questions, such as the presence of fever, dyspnea, or risk factors for infection, are often used to select patients that require isolation until a COVID-19 test.[72] However, overlap between chest pain and these symptoms in addition to concerns regarding COVID-19-related causes of chest pain means that many chest pain presentations still require initial isolation.

Follow-up for chest pain presentations more commonly occurred via telehealth, which is limited by the absence of in-person environment and physical examination.[73] Finally, patient presentation rates for many conditions, including ACS, were observed to decrease during periods of high community prevalence in the setting of patient concerns regarding overburdening health systems under strain or the risk of contracting COVID-19 while in hospital.[74]

Many of the challenges with chest pain care models in the setting of COVID-19 have improved as community prevalence has decreased with widespread vaccine availability. Access to rapid antigen testing may have reduced some delays to evaluation and management. Modifications to existing chest pain CDPs that consider the need for COVID-19 testing and isolation precautions are worthwhile to streamline care models and prioritize early ECG for rapid identification of STEMI.[75] Similarly, public health education to encourage patients with acute chest pain to contact EMS or present to EDs might allay some fears regarding presentation.

SYSTEM AND PATIENT IMPACTS OF EXISTING ASSESSMENT PATHWAYS

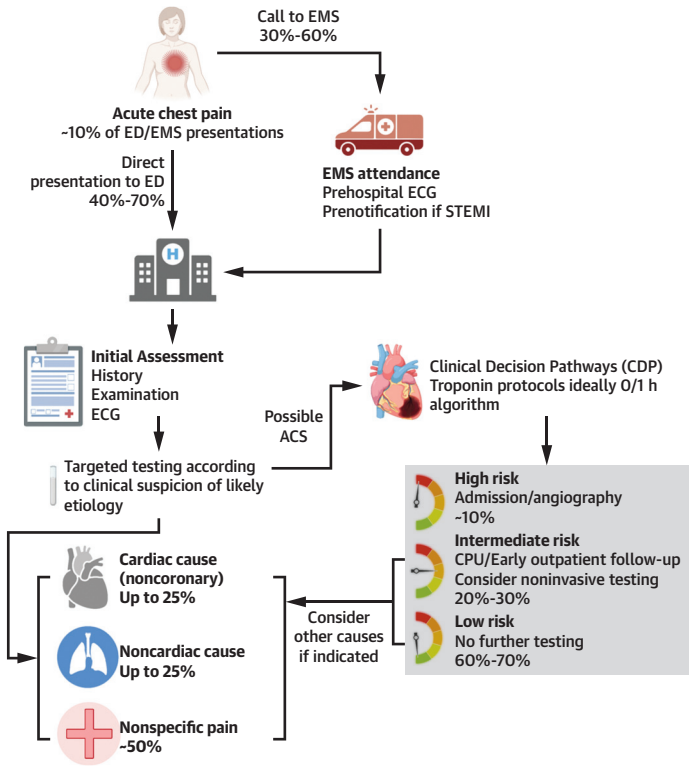
The patient and system impacts of assessment pathways are summarized in this section and include high financial costs among patients often classified as low risk, system overcrowding and delays in treatment and diagnosis for other patients, the impost of prolonged assessment and admission times on patients, and harms relating to overinvestigation (**Figure 4**).

FINANCIAL COSTS OF ACUTE CHEST PAIN CARE. Each aspect of acute chest pain assessment—including prehospital transfer (often requiring specialized staff), emergency assessments and subsequent cardiac investigations, and management for high- or intermediate-risk patients—is associated with costs. In 2015, an Australian study estimated mean ED and admission costs for acute chest pain attendances at AU$13,509 (US$9,854) for patients diagnosed with ACS, AU$7,283 (US$5,314) for other cardiovascular conditions, and AU$3,331 (US$2,430) for noncardiac conditions,[76] with similar estimates in other jurisdictions.[77,78] In the United States, mean costs in 2016 per acute chest pain attendance to ED were estimated at US$6,325, with a total annual cost of US$1.5 billion.[79] Rapid testing protocols and adherence to chest pain pathway protocols are associated with reductions in hospital costs.[80-83] In 1 study, the introduction of an accelerated diagnostic protocol across 16 hospitals in Australia resulted in a AU$13.5 million (US$9.8 million) saving through a 20% reduction in ED length of stay (AU$2.3 million saving) and a 13% reduction in hospital admissions (AU$11.2 million saving).[84] The introduction of highly sensitive troponin assays has been associated with improved early rule-out processes, reduced need for functional testing, and a mean 20% reduction in costs.[85] Noninvasive anatomical or functional tests are a significant driver of high costs. However, despite these costs, some studies have suggested that early use of imaging in intermediate-risk patients may be cost effective by facilitating earlier discharge and reduced subsequent invasive angiography.[86-90] Benefits of early noninvasive testing in low-risk patients are less clear, especially in the setting of highly sensitive troponin assays.[91,92]

IMPACTS ON HEALTH SYSTEMS. Acute chest pain attendances are frequently associated with rates of hospital admission ranging from 40%-70%.[38,39] Although assessment times are improving with highly sensitive troponin assays and protocolized chest pain pathways, the burden on systems remains significant. Overcrowding in EDs in the setting of hospital access block has become increasingly common in many jurisdictions and is associated with increased costs, delays to treatment, worsened patient outcomes, cancellation of elective procedures, delays in ambulance off-load times, and in turn, delays to ambulance response times.[91,93-95] Acute chest pain, accounting for 10% of ED attendances, remains a significant driver of this problem, and even small improvements in ED or hospital admission times have the potential to reduce overcrowding and improve overall health care quality.[36,96]

RISKS OF OVERINVESTIGATION AND OVERTRIAGE. Low-risk categorization in acute chest pain patients generally aims to represent an ACS "miss" rate of ≤1%, consistent with the expectations of >50% of clinicians that ACS diagnostic strategies should achieve a sensitivity of 99% or higher.[97] However, increased sensitivity needs to be balanced against the risk of harms associated with false-positive testing and overinvestigation, sometimes termed the test threshold.[98] In the setting of contemporary troponin assays, this has been estimated at 2% (ie, it is estimated to be worthwhile undertaking troponin testing if the pretest probability is >1 in 50).[98] Conversely, indiscriminate troponin testing can lead to diagnostic uncertainty and unnecessary investigations.[99] Similarly indiscriminate noninvasive imaging investigations for low-risk patients with chest pain leads to increased costs and system burden, higher rates of invasive angiography (and associated patient risks), with little evidence to suggest improvements

FIGURE 4 Problems With Existing Acute Chest Pain Care Models



Left panel shows the structure of existing acute chest pain care models including rates of presentation and final etiology. The **right panel in blue** identifies problems with existing models of care in regard to patient care and outcomes, and the burden on health systems. ACS = acute coronary syndrome; CPU = chest pain unit; ECG = electrocardiogram; ED = emergency department; EMS = emergency medical services; STEMI = ST-segment elevation myocardial infarction.

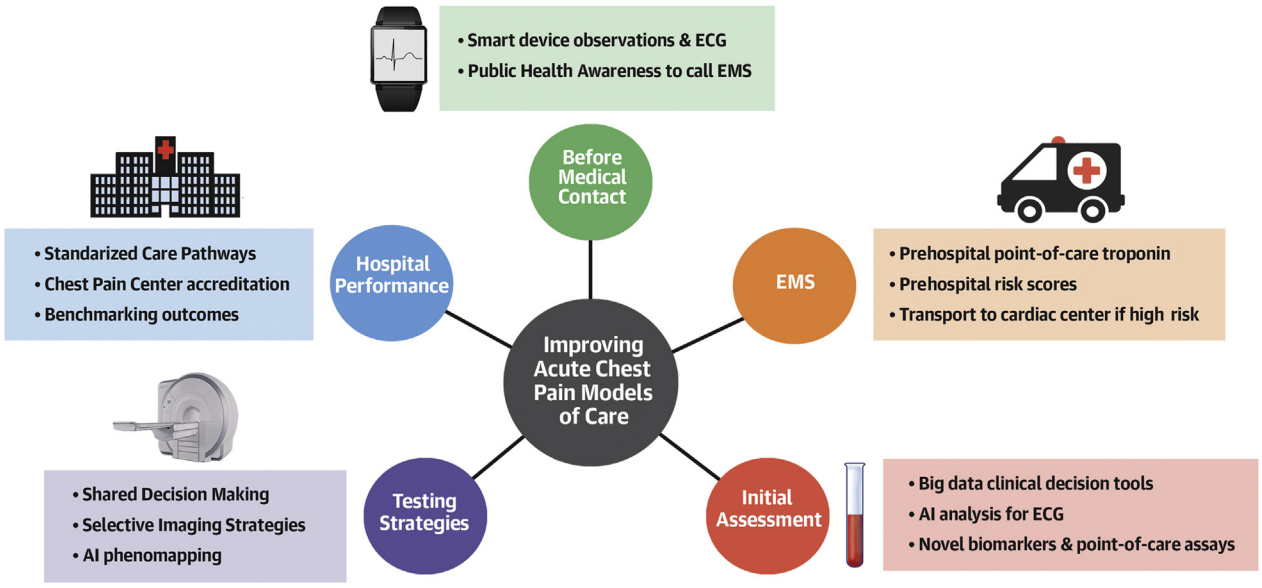
in diagnosis rates of coronary artery disease or improvements on outcomes.[92,100,101] Furthermore, in 1 study, higher clinician-specific hospitalization rates for acute chest pain were not associated with improvements in 30-day outcomes, suggesting that an overly conservative approach to acute chest pain management resulting in a lower threshold for admission is not necessarily safer.[102]

IMPROVING ACUTE CHEST PAIN MODELS OF CARE

Novel research into improving models of acute chest pain evaluation is of great importance in both improving patient outcomes and reducing the burden and costs of lengthy acute chest pain assessment processes. There is substantial scope for improvements in speed of diagnosis and risk stratification methods given that the vast majority of patients are eventually safely discharged home. This section focuses on developing research that might safely improve both the speed of care and tools available to diagnose and manage patients with chest pain without increasing the risk of adverse events (Central Illustration).

NOVEL TECHNOLOGIES FOR RISK STRATIFICATION BEFORE MEDICAL CONTACT. Just as parts of usual ED care are being shifted to prehospital EMS care, similar developments in technologies might provide patients and clinicians with clinical information before arrival of medical personnel. Smartwatch and mobile devices that can monitor arrhythmias, including atrial fibrillation, have seen significant advances in the last decade, and research in this area has expanded to assessment of ischemia.[103] Home ECG monitoring devices, such as the AliveCor device,[104] have demonstrated usefulness in detecting ischemia and acute ST changes.[105] Nine-lead ECGs are obtainable with some smartwatches, including the Apple Watch, by placing the smart watch on different positions on the body, and have been used to detect ischemia with comparable results to standard ECGs.[106,107] Similarly, smart phone and watch tools to

CENTRAL ILLUSTRATION **Improving Acute Chest Pain Models of Care**



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Novel areas of research and development that might translate to improved patient and system outcomes for acute chest pain presentations. AI = artificial intelligence; ECG = electrocardiogram; EMS = emergency medical services.

detect arrhythmias have been approved by the U.S. Food and Drug Administration, which also may provide useful information to patients and clinicians before medical contact, given acute chest pain relates to arrhythmias in a proportion of cases.

Developments in smart devices also include clinical observations, such as pulse oximetry, blood pressure, and heart rate, with similar accuracy to commercial purpose-specific devices.[108] With these developments, it might be feasible for patients with acute chest pain to contact EMS and transmit a full set of observations, and ECG rhythm and ischemia data to assist in early risk stratification and triage decisions, and prioritize EMS attendance to patients with life-threatening conditions such as STEMI. However, it is important to note that for existing devices, variability between devices and between activity types have been observed, with 1 study demonstrating an average error rate 30% higher during activity compared with rest for wearable heart rate sensors.[109]

EMS RISK STRATIFICATION AND PREHOSPITAL POINT-OF-CARE TROPONIN ASSAYS. Improvements in prehospital care of acute chest pain, including the use of ECGs and prenotification for STEMI, have resulted in improved outcomes among chest pain cohorts and these are now established standards of care.[18] Success with these interventions has prompted research into further avenues for improvement, including the use of prehospital risk stratification, use of point-of-care troponin assays, and improved ECG algorithms.

Several studies have assessed the feasibility of incorporating paramedic-based risk assessments using risk stratification scores, that might ordinarily be used by clinicians in EDs, often in combination with point-of-care troponin sampling. Overall, the process of troponin sampling and risk score calculation (eg, HEART score) has been shown to be feasibly performed by paramedics and is associated with reduced ED length of stay.[110-116] Studies to date have been performed using contemporary troponin assays, which may not safely rule out ACS,[115] but highly sensitive point-of-care troponin assays are in development by several companies and likely to be available for use in the prehospital setting in the near future. For the 30%-60% of patients arriving to ED with acute chest pain via EMS, routine use of risk stratification and point-of-care highly sensitive troponin sampling would allow patients to arrive to

ED with a completed HEART score, potentially allowing early discharge for low-risk patients within the first hour after a second troponin is sampled or consideration of alternate diagnoses. Conversely, high-risk patients with an initially elevated troponin could assist in guiding prehospital management, especially aspirin administration, intravenous access, transport urgency decisions, and decisions to directly transport patients to catheterization-capable centers, avoiding interhospital transfers. Similarly, on arrival to ED, an elevated troponin result would assist in guiding ED triage categorization, and decisions regarding early evaluation and management, and might facilitate earlier decisions regarding disposition from the ED. Some studies have suggested paramedic risk stratification and point-of-care troponin results could occur at the patient's home with only patients at intermediate or high risk transferred to hospital,[116] but this may be somewhat optimistic without a risk assessment process to exclude other serious conditions such as pulmonary emboli, pneumonia, and acute aortic pathologies. Further trials assessing these processes are planned.[117,118]

RISK STRATIFICATION MODELS, BIG DATA, AND MACHINE LEARNING. Existing risk stratification scores for acute chest pain are mostly variations on simple counting tools, similar to the CHA_2DS_2-VASc score for stroke risk in atrial fibrillation, which facilitate ease of use clinically. However, these tools do not quantify absolute risk in the way that more complex models incorporating more variables do, such as the QStroke score, which demonstrates substantially improved discrimination for stroke risk in AF patients compared with the CHA_2DS_2-VASc score, or the numerous mortality predictive models used for risk adjustment in cardiovascular procedural registries.[119,120] Electronic medical records systems are now widespread and provide opportunities to incorporate more complex models into standard clinical processes, which might more accurately quantify risk in comparison to simple counting tools such as the HEART score.[121,122] Greater availability of large linked clinical and administrative datasets provide similar opportunities for developing enhanced risk prediction models. Moreover, predictive models that can stratify risk of serious non-ACS causes of chest pain, may assist in determining the need for noncoronary investigations and safety of early discharge among patients with normal serial highly sensitive troponin assays.

Machine learning and artificial intelligence methods have been well-publicized across clinical medicine in recent years, and several studies have demonstrated potentially promising applications in prediction modeling, disease phenotyping, image interpretation (including ECGs and radiology), and precision medicine.[123] In stable chest pain, a phenomapping-derived tool was used in the PROMISE (PROspective Multicenter Imaging Study for Evaluation of Chest Pain) and SCOT-HEART (Scottish COmputed Tomography of the HEART Trial) populations to select phenotypic neighborhoods favoring anatomical or functional testing, demonstrating a lower incidence of MACE using the tool's recommended testing strategy.[124] Deep learning-based artificial intelligence algorithms have demonstrated excellent discrimination for diagnosing MI using 6- or 12-lead ECGs,[125] with improvements in sensitivity of 52% compared with commercial interpretation software and 37% compared with experienced clinicians in 1 study.[126,127] Multiple studies have assessed the use of artificial intelligence in predicting diagnosis or outcomes in chest pain cohorts using artificial neural networks, random forest, support vector machine, and gradient boosting methods, and although these have generally outperformed clinicians and existing risk stratification tools, few have yet been incorporated into practice.[128,129] Similarly, although these methods potentially show promise, whether performance in chest pain predictive modeling improves on more conventional statistical methods such as logistic regression is not yet clear.[130,131]

NOVEL BIOMARKERS. Troponin assays predominate assessment of patients with suspected ACS, but several novel biomarkers are potentially promising and warrant mention, including cardiac myosin-binding protein C (cMyC) and noncoding RNAs (ncRNAs). cMyC, a sarcomeric protein associated with myosin and actin, can be detected earlier in blood and rises more rapidly in comparison to troponin.[132] In undifferentiated chest pain patients presenting to ED, cMyC at presentation provided comparable discriminatory power (area under the curve: 0.924) in comparison to a single highly sensitive troponin assay, and led to improved discrimination when combined with highly sensitive troponin assays.[133] ncRNAs include microRNAs, circular RNAs, and long noncoding RNAs, and although sensitivity of current ncRNAs is inferior to troponin assays, research into potential combined biomarkers using miRNA and cMyC is ongoing.[134,135] Furthermore, some biomarkers such as copeptin, midregional proatrial natriuretic peptide, C-terminal proendothelin-1, midregional proedrenomedullin, and procalcitonin may assist in differentiating type 2 MI from type 1 MI in chest pain cohorts.[136,137]

Perhaps of greater importance in the near future are improvements in point-of-care devices and troponin assays. Rapid point-of-care highly sensitive troponin assays that provide results in <15 minutes have been developed but are not yet widely available for clinical use.[138] Such assays are likely to improve ED length of stay, especially using the 0/1-hour troponin pathway, which would be able to classify patients as low risk with increased speed compared with awaiting results from current, slower, lab-based assays.

UPFRONT NONINVASIVE IMAGING STRATEGIES. A complete discussion of noninvasive imaging strategies in ED and index admission of patients with acute chest pain is outside the scope of this review, but numerous studies have assessed the impact of different imaging strategies on patient outcomes and cost effectiveness. Upfront strategies (following troponin and ECG but before invasive angiography) for several modalities, including computed tomography (CT) coronary angiography (CTCA), have been associated with improved cost effectiveness in acute chest pain cohorts.[139] The ACRIN-PA (CT Coronary Angiogram Versus Traditional Care in Emergency Department Assessment of Potential ACS) and ROMICAT-II (Multicenter Study to Rule Out Myocardial Infarction by Cardiac Computed Tomography) trials demonstrated that CTCA reduced ED length of stay and increased ED discharge rates in comparison to inpatient functional testing.[140,141] However, a routine noninvasive imaging strategy before discharge has not been demonstrated to improve early outcomes, and in the ROMICAT-II trial, was associated with increased downstream testing and radiation exposure.[142] Moreover, the BEACON (Better Evaluation of Acute Chest Pain with Computed Tomography Angiography) trial, which was performed in the highly sensitive troponin era, found that although overall costs were lower due to reduced outpatient testing, there was no added benefit of additional testing over highly sensitive troponin assays in identifying significant coronary disease.[143] Therefore, the use of these tests needs to be carefully selected and may be most suited to intermediate-risk rather than low-risk patients.[91,92,139]

Although the use of imaging in low- and intermediate-risk patients has been extensively studied, potential new applications for developing techniques might include upfront imaging to assess selected high-risk patients and those with elevated troponin values. Invasive angiography has been the gold-standard investigation for high-risk patients for over 2 decades and allows treatment with percutaneous coronary intervention at the time if required. However, up to 50% of patients undergoing angiography for non-STEMI do not require revascularization, and 5%-10% are better managed with bypass surgery—both groups that might avoid complications associated with invasive angiography if noninvasive workup could be done safely and accurately without delaying revascularization.[144] An initial imaging-guided strategy in non-STEMI was associated with a 44% reduction in invasive angiography use for patients initially undergoing CTCA and an 13% reduction in patients undergoing CMR in comparison to conventional angiography first pathways, with no increase in 1-year MACE.[145] Similar findings were identified in the VERDICT (Very Early Versus Deferred Invasive Evaluation Using Computerized Tomography in Patients With Acute Coronary Syndromes) trial, which demonstrated high diagnostic accuracy to rule out clinically significant coronary disease using upfront CTCA in patients with non-ST-segment elevation acute coronary syndromes, potentially avoiding unnecessary invasive testing in some patients.[146] Nonetheless, invasive angiography remains the best approach for high-risk patients, and further large studies would be required before a shift toward noninvasive strategies could be recommended. Similarly, further data assessing whether CT imaging (including fractional flow reserve and perfusion) can be used to accurately guide revascularization decisions, rather than simply acting as a gate-keeping test to angiography, would also be required.

PATIENT–CLINICIAN SHARED DECISION-MAKING. Clinician concern regarding missed diagnoses often results in a risk averse approach to chest pain workup including admission to CPUs and further diagnostic testing of low-risk patients. This can result in increased downstream procedures and higher costs without necessarily improving outcomes. A growing body of evidence has demonstrated that patient-clinician shared decision-making results in greater patient education, lower rates of CPU admission, lower rates of unnecessary diagnostic testing, and is not associated with higher rates of MACE.[147,148] Shared decision-making aids are useful across a variety of decision contexts, and can reinforce the importance of outpatient follow-up, effectively educate patients regarding their individual risk, and facilitate timely discharge.[149] Recent chest pain guidelines recommend decision aids for both low-risk patients to facilitate risk communication, and intermediate-risk patients to assist in shared decisions surrounding further inpatient or outpatient

investigations and the need for admission, observation, or discharge.[1]

BENCHMARKING AND MONITORING HOSPITAL PERFORMANCE. Clinical quality registries have proliferated over the last 2 decades, and many countries and localities now monitor hospital and operator performance in cardiovascular procedures through such registries.[150] In the United States, the Chest Pain-MI registry has been developed to standardize chest pain and MI hospital-based care,[151] but few registries using a symptom-based rather than disease-based (ie, MI or ACS) approach have been developed elsewhere. Chest pain center accreditation is offered by the American College of Cardiology in the United States with the goal of helping hospitals to identify and improve care for patients with suspected ACS, with reaccreditation required every 3-5 years, which may be an effective mechanism for improving outcomes.[152,153] This accreditation process has been taken up widely in the United States in addition to some other countries, including China.[55] As availability of electronic record systems, administrative databases, and linkage processes improve, benchmarking and monitoring of hospital (and prehospital) performance by measuring chest pain-specific key performance indicators and risk-adjusted outcomes (as is done for percutaneous coronary intervention registries) might assist in standardizing hospital care and identifying outlier hospitals where care processes can be improved.[151] A similar approach might also be applicable to avoid excess costs and overtesting among low-risk chest pain presentations. For example, risk-adjusted key performance indicators might be developed using linked dataset that monitor institutional costs, rates of imaging, and adherence to CDPs for acute chest pain presentations.

CONCLUSIONS

Patients with acute chest pain are common and current assessment pathways frequently include prolonged ED and hospital admissions with a focus on exclusion of ACS with high certainty, contributing to health care costs, hospital overcrowding, and sometimes over-investigation. There are multiple avenues to improve existing models of chest pain evaluation including novel risk stratification pathways incorporating highly sensitive point-of-care troponin assays, in both the hospital and prehospital setting; public education surrounding new technologies such as smartwatches' ongoing development into indications for further testing including the use of developing artificial intelligence and precision medicine methods; increased uptake of CDPs, CPUs, and accreditation programs; and improved hospital benchmarking and performance monitoring for acute chest pain attendances to standardize care. Improving the speed and accuracy of chest pain diagnosis and management is likely to translate to significant benefits for patients and health systems.

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APPENDIX For supplemental tables, please see the online version of this paper.