Low-Risk Chest Pain: Can We Omit Non-Invasive Imaging?

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Acute chest pain is a leading cause of emergency department (ED) admission and hospitalization. Early risk assessment is the key for proper triage and management in such patients. Accordingly, current guidelines recommend rapid clinical, electrocardiogram (ECG), and laboratory evaluation, including cardiac troponin (cTn) levels [1]. Further risk stratification and early invasive therapy within 2–72 hours are recommended in the presence of various high-risk clinical, electrocardiographic, or laboratory features such as heart failure, arrhythmia, rise and fall of cTn, or left ventricular systolic dysfunction. In contrast, low risk patients should be managed more conservatively and be referred for a non-invasive test.

In recent years, the introduction of high-sensitivity cardiac troponin (hsTnI) measurements enabled faster and more accurate diagnosis of acute myocardial infarction [2,3], resulting in reclassification of a substantial proportion of unstable angina patients to non-ST-elevation myocardial infarction (NSTEMI) [4,5], thereby reducing the group of low-risk patients who have better outcome compared with NSTEMI patients [6]. The remaining challenge in such low risk patients is the early identification of those who are at a sufficiently low risk to be discharged from the ED without further testing.

In this issue of *Israel Medical Association Journal* (*IMAJ*), Marcusohn et al. [7] presented a retrospective analysis questioning the traditional low-risk pathway and suggest omitting non-invasive testing altogether. The results from 52 low-risk patients with normal cTn on serial testing showed no abnormalities on myocardial perfusion imaging (MPI) in patients with low-risk non-ST-elevation acute coronary syndrome (NSTE-ACS) diagnosed with unstable angina. The authors concluded that hsTn could serve as a single prognostic marker and improve classification and management of patients without requiring additional tests to rule out coronary artery disease.

This thought-provoking notion has potentially important implications for triage, hospitalization time, and costs for healthcare systems, which may carry significant benefits for the system and patients. However, several caveats should be considered before non-invasive testing is omitted in this group.

The main limitation of the current study is its very small sample size. As the prevalence of significant ischemia in these low-risk patients is low, but not negligible, the study is underpowered to reliably lead to the conclusion that noninvasive testing can be routinely omitted in such patients. This limitation seriously impedes the study's ability to exclude significant ischemia. When extrapolating from stable angina patients, revascularization is indicated in cases with large ischemic territory for prognosis [8]. This recommendation is based on studies showing improved outcome in such patients [9]. Evaluation of ischemic burden cannot be accurately performed by clinical judgment or blood tests and requires further imaging such as MPI. Chest pain can be challenging to classify, with many ACS patients presenting with atypical rather than typical chest pain [10]. Therefore, substantial intra- and inter-observer variability exists in categorization of pain type. Furthermore, low risk chest pain patients vary in their pretest probability of disease, which should impact clinical decision pathways. Among patients with a high pretest probability, greater caution is warranted [11]. To address this issue, a number of clinical risk scores, most notably the HEART score, were developed and validated. These scores incorporate various parameters including history, ECG, age, risk factors, and initial troponin levels. They have been shown to successfully identify patients at very low risk who can safely be discharged from the ED [12,13] and those who require further testing [14].

The HEART score was developed and validated for patients with chest pain, while the GRACE score, used in the current study, as well as the TIMI score, were developed and validated for patients with confirmed MI. Therefore, the HEART score would have been more appropriate for the population studied by Marcusohn et al. [7]. In fact, the HEART score has been shown to improve the negative predictive value of a negative troponin based pathway [15]. It would, therefore, be more prudent to rely on the combination of a low (< 3) HEART score in conjunction with a negative HsTn assay to decide on early discharge.

There is no doubt that triage decisions should be individualized, based on all available clinical and laboratory information. By relying on any single parameter, the risk of misdiagnosis and consequently an adverse patient outcome is increased. NSTE-ACS patients at higher risk clearly benefit from early invasive assessment and intervention [13].

As clinicians, we should rely on evidence-based data and current guidelines when treating patients, while striving to personalize our management for our patient. In patients with chest pain this can only be achieved by incorporating careful

history with all prior information, preferably using a validated risk score and including of course a high sensitivity troponin assay used according to a validated rule out and rule in protocol.

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Capsule

Fat switches melanomas to metastasis

Melanomas proliferate in the upper epidermal layer of the skin and become invasive when they grow into the deeper layers containing adipose tissue. **Golan** et al. found that adipocytes promoted this metastatic switch by secreting cytokines that repressed the expression of a microRNA in melanoma cells. This microRNA promotes proliferative phenotypes and suppresses invasive phenotypes. It appears to do this by repressing the expression of a receptor for transforming growth factor β, which is implicated in metastasis that is abundant in the dermal layer.

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Capsule

Early insulin recognition by T cells

Type 1 diabetes is initiated by loss of T cell tolerance to pancreatic islet autoantigens, including insulin. **Gioia** and colleagues developed major histocompatibility complex (MHC)-peptide conjugates capable of distinguishing populations of insulin-reactive CD4+ T cells from diabetes-prone mice. These reagents differ in the register used for insulin peptide binding to class II MHC. Analysis of pancreatic islet tissue revealed that the earliest phase of the anti-insulin T cell response in islets is dominated by T cells that recognize an insulin$_{12–20}$ peptide–MHC class II complex. Identification of the primary mode of peptide recognition used by the early anti-insulin T cells opens the door to designing inhibitors capable of selectively blocking activation of these rogue T cells.

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"Any intelligent fool can make things bigger, more complex, and more violent. It takes a touch of genius – and a lot of courage – to move in the opposite direction"

Albert Einstein (1879–1955), German-born theoretical physicist who developed the theory of relativity, one of the two pillars of modern physics (alongside quantum mechanics)