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Editorial

Prolonged Reperfusion Delays During the COVID-19 Pandemic: Is Faster Always Better?

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See article by Mahli et al., pages 783–791 of this issue.

The treatment of ST-segment elevation myocardial infarction (STEMI) has evolved greatly over the past decades, moving from medical management only to fibrinolysis and finally to primary percutaneous coronary intervention (PPCI). The improvements in all aspects of the management led to decreases in hospital and longer-term mortality.[1,2] While medical management and advances in device therapies played a crucial role, one of the key factors of treatment is widely considered to be the delay from first medical contact to opening of the culprit artery (FMC-to-device delay), because "time is muscle" with STEMI.[3,4] Subgroup analyses from large randomised clinical trials and observational studies showed a direct relationship between reduced FMC-to-device delay and improved clinical outcomes, including a reduction in mortality.[5-8] As such, all efforts have been directed toward reducing this delay, notably by creating new emergency medical service pathways. The first regional protocol for patient transfer to a PPCI-capable centre was developed in Canada.[9] Owing to these new measures, FMC-to-device delays have decreased considerably over the past 15 to 20 years.[10,11]

The COVID-19 pandemic brought a whole new burden to health care systems around the globe. The Canadian health care system sustained significant burnout, with COVID-19 patients occupying coronary or intensive care unit beds and a shortage of health care workers. The pandemic, in its most intense periods, limited the capacity of tertiary care hospitals to accommodate transfers, which caused treatment delays in patients with cardiac and other diseases.[12] The treatment of STEMIs, despite its emergency nature, was inevitably affected by those factors. Many registries and meta-analyses confirmed the overall impression in catheterisation laboratories around the world: The number of STEMI patients reaching the hospital and the catheterisation laboratory declined and STEMI patients' treatment was often delayed.[13-18]

In this issue of the *Canadian Journal of Cardiology*, Mahli et al. add to the growing body of literature on STEMI treatment during the COVID-19 pandemic.[19] In this study from British Columbia, the incidence of STEMI patients treated with PPCI remained the same compared with previous years, in contrast to previously published data from Canada and other countries, which reported a reduction in those numbers.[14,15,17,18] The pandemic hit British Columbia much later than other parts of Canada, with a first wave in the early fall of 2020,[20] which likely preserved the natural propensity of patients to seek medical attention when they were symptomatic with STEMI. A total of 949 STEMI patients treated during the same period of the year over the 3 years preceding the pandemic were compared with 305 patients treated during COVID-19. Over the study period, FMC-to-device delay rose from 102 minutes to 116 minutes, a significant 14-minute increase (interquartile range [IQR] +8 to +20 minutes) that was even more pronounced in patients requiring transfer to a PPCI-capable centre, for which the delay went from 117 to 145 minutes, almost half an hour more (IQR +16 to +38 minutes). Similar delays in treatment during the pandemic were observed in previous registries and meta-analyses as well, with increases in door-to-balloon time averaging around 10 minutes.[13,14] Interestingly, the number of mechanical complications was the same as before the pandemic. However, mortality was lower by an absolute 2.4% during COVID-19. Although this difference in mortality was not significant (with a P value of 0.18), authors could have been tempted to attribute an increase in mortality of a similar magnitude to treatment delays.

Should we be surprised that mortality was not affected by such an increase in treatment delays? Not so much. Using the CathPCI Registry of the National Cardiovascular Data Registry, Menees et al. analysed 96,738 admissions for PPCI and showed that in-hospital and 30-day mortality remained unchanged despite a 19% decrease in US door-to-balloon time (from a median of 83 to 67 minutes) from July 2005 to June 2009.[11] Moreover, this finding was consistent in all

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subgroups, including the high-risk ones such as elderly, anterior MI, and cardiogenic shock patients. In the **St**rategic **R**eperfusion **E**arly **A**fter **M**yocardial Infarction (STREAM) trial, which compared fibrinolysis and PPCI in patients who could not undergo PPCI within 60 minutes, randomisation to a reperfusion therapy that had an inherent 78-minute delay did not cause any harm. Although we should acknowledge that fibrinolysis is successful in only two-thirds of patients, that study gives some clues that a reasonable delay in reperfusion might not be as harmful as previously thought.[21]

The excellent article by Mahli et al. is the first to report the impact of an increase in FMC-to-balloon delays on in-hospital mortality in the current era of fast and well drilled reperfusion protocols. COVID-19 served as a natural experiment that reversed temporal trends in improvement of treatment delays in STEMI. Longer FMC-to-reperfusion delays are inevitably associated with numerous biases and confounding factors in observational studies: Patients in shock, patients with pulmonary edema, older patients, and patients with vascular disease may experience delay in treatment owing to their poor condition. Attributing the increase in mortality to the delay itself rather than those comorbidities requires statistical control of those confounding factors. However, in statistical analyses, one can only control for known confounders, while unmeasured ones likely remain in the relationship between shorter reperfusion delays and reduced mortality. Nevertheless, over the past 20 years, the FMC-to-device delay has been regarded as the primary quality-of-care metric in STEMI patients. This is reinforced in practice guidelines stating that STEMI patients should receive PPCI within 90 to 120 minutes, depending on the centre at which they present.[3,4] Everyone in cardiology believes that the sooner the occluded artery is reopened, stopping the transmural lesion current and limiting the irreversible infarct size, the better the outcomes will be. While there is no doubt that STEMI treatment is an emergency and that the benefits of PPCI over fibrinolysis is dependent on the FMC-to-device delay, taking extra minutes once PPCI has been chosen may not be as harmful as we thought.[22-26] While FMC-to-treatment delays are considered fundamental and dogmatic metrics for quality of care, one might wonder whether other, more meaningful, outcome measures or care processes, such as risk-adjusted short-term mortality, completeness of revascularisation, or use of guideline-recommended therapies, should take over in our assessment of quality of care in STEMI. Taking extra minutes to take a good clinical history, ruling out contraindications and listening to the heart to rule out major murmurs, organise a safer transfer of a patient, explore alternative diagnoses, assess local resources before transfer with a nurse or a physician (and therefore avoiding harming other patients), treat pulmonary edema, and stabilise blood pressure are examples of things are likely worth doing instead of rushing to meet the delay-to-reperfusion goals. Optimising therapy once in hospital is likely as important as time to reperfusion. This involves non−infarct-related artery PCI for complete revascularisation, prompt recognition of mechanical complications, and up-to-date management of cardiogenic shock. With the establishment of new COVID-19 protocols, the assessment and care of patients became unquestionably more systematic. While the observed reduction in mortality after PCI could have been partially explained by a reduction in patients' risk profile once reaching the catheterisation laboratory, the data do not support this hypothesis, with similar risk profiles of both cohorts.

Obviously and rightfully, no investigator will ever randomise patients to longer vs shorter FMC-to-device delay. The COVID-19 pandemic gave us the unexpected natural experiment to measure the effect of moderately prolonged FMC-to-device delays on clinical outcomes after STEMI. It is time to reassess the quality indicators of STEMI programs. Faster is not always better.

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