Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

to micromolecules, and the structural changes induced by hypertension could affect molecules differently depending on size and mechanism of transport. It is possible that the arterial changes also affected the transport of small molecules, including water, into the intima and through the arterial wall, but we did not examine that. The question would also be interesting to examine closer in the future.

Finally, Drs. Wang and Ge note that "atherosclerosis of the aorta should not be milder than that of the coronary arteries." Increased blood pressure is but one factor fueling atherogenesis. Multiple other factors, including arterial structure, cellular composition, and hemodynamic properties, determine the susceptibility of vascular territories to offending risk factors. The severe atherosclerosis that we observed in the coronaries was, therefore, the result of exposure to hypertension and the generally high predisposition of this arterial bed toward atherogenesis. As in humans, the pig thoracic aorta was more resilient.

Dr. Aslanger raises an interesting hypothesis regarding how flow may explain our observations. We aimed to isolate the direct effect of hemodynamic factors versus humoral factors in hypertension and showed that accelerated atherogenesis occurred in areas of high pressure but not low pressure in the same animals. We also showed that a contributing mechanism may be increased intimal LDL accumulation, which could reflect proteoglycan-mediated binding or hindered passage of macromolecules across the artery wall due to restructuring (1). The mechanisms connecting pressure to these changes remain, however, to be explored. Hypertension-induced alteration in flow velocity and pattern, as suggested by Dr. Aslanger, leading to local changes in shear stress is certainly a hypothesis with merit and should be examined in future research.

Dr. Aslanger also points out that absolute pressures do not predict the rate of atherogenesis across the body. Importantly, this is not the same as to say that increases in pressures may not be proatherogenic. Under physiologic conditions, each artery is developed to cope with the particular local pressures and lumen diameters that are needed for distribution of blood. The guiding principle is to keep the load on arterial smooth muscle cells constant by varying the number of these cells (2). Thus, arterial cells do not sense the absolute luminal pressure, but will sense relative increases in pressure that will increase tensile stress and require restructuring of the arterial wall to normalize the mechanical load per cell. We propose that these restructuring processes, detected by histology and proteomics in our experiment, are at the heart of hypertension-accelerated atherogenesis.

In conclusion, at this stage we are left with more questions than answers. Future experiments will tell which path the story will take.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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Collateral Casualties of COVID-19

We read with interest the recent paper by Einstein et al. (1). During the coronavirus disease 2019 pandemic, a rapid reduction in cardiovascular diagnostic procedures was observed globally with a potential impact in the care of millions of patients. From the early stages of the crisis, concerns have been raised about the very real potential for "collateral casualties" of the pandemic: people who never contracted severe acute respiratory syndrome coronavirus 2 but died from noninfectious causes sooner than they would have under normal circumstances.

Similarly, the impact of the pandemic on the endoscopic procedures and its effect on gastrointestinal cancer detection was recently investigated in a large retrospective study from 15 endoscopic

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units in the Netherlands (2). In a country proud of its national screening program, Latinga et al. (2) found that gastroscopies decreased by a staggering 57% and colonoscopies by 45%, with a subsequent reduction in the number of gastrointestinal cancers detected. Similar disappointing results were seen in a national study in the United Kingdom (3). Early in the United Kingdom's response to the pandemic, endoscopy activity reduced to just 5% of normal activity, and 10 weeks later activity had increased to only 20% of pre-pandemic levels. Endoscopic cancer detection decreased by 58%, and colorectal cancer detection by 72% (3). Of course, this is going to have far-reaching consequences in terms of future cancer survival.

This is only the tip of the iceberg; the total number of collateral casualties will eventually be higher than the coronavirus disease 2019 deaths. The speed of recovery of diagnostic activities across the board will determine the scale of the collateral damage. The time is ripe for a collective overview of all aspects of the pandemic's impact on current health care delivery and the roll-out of telemedicine solutions.

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REPLY: Collateral Casualties of COVID-19

We appreciate the thoughtful comments by Dr. Koulaouzidis and colleagues and are in fundamental agreement. Indeed coronavirus disease 2019 (COVID-19)'s "collateral casualties" may well surpass its direct mortality. Nowhere is this more important than for cardiovascular diseases, the leading cause of mortality worldwide, which account for approximately 18 million deaths annually even with health care delivery not curtailed by the pandemic response. The dramatic reduction in evaluations for cardiovascular disease at the beginning of the pandemic that we observed in the INCAPS COVID (International Atomic Energy Agency Noninvasive Cardiology Protocols Study of COVID-19) (1) begs the need for aggressive efforts to identify and reach patients who have missed cardiac care, including coordinated efforts at catch up for studies missed.

As Dr. Koulaouzidis and colleagues emphasize, a similar phenomenon has been described for the gastrointestinal cancer detection field, where they have made important contributions to characterizing the pandemic-associated drop in diagnostic testing and screening. Clearly this problem vexes other types of cancer, too, with mammography screening hit especially hard (2). National Cancer Institute Director Norman Sharpless has predicted, based on modeling, a ~1% increase in breast and colon cancer mortality, representing >10,000 excess deaths in the United States, due to missed screening and treatment during the pandemic, and reports as well an unprecedented disruption of cancer clinical trials (3). A similar disruption of the cardiovascular clinical trial landscape has been described, with problems including suspended trials, missed and postponed trial-related assessments hindering data quality, heterogeneity in data collection, underpowered outcome analyses from lowered event rates related to patients' avoiding the health care system, and, conversely, inflated mortality endpoints (4).

Thus, across the health care enterprise, and for cardiovascular disease in particular, COVID-19 continues to wreak collateral casualties in diagnosis, screening, treatment, research, and education. The magnitude of these problems beyond the initial phase of the pandemic is less well understood and will be characterized in the worldwide INCAPS COVID 2 study, which is planning to collect data in May 2021; those interested in participating are cordially invited to send an e-mail in that regard to INCAPS.Contact-Point@iaea.org. It is incumbent on the cardiovascular community—as for other communities, such as cancer—to