angiography. Small sample size of the coronary angiography group (n = 9) in the present report might be the cause of this insignificance.

References


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Acute chromosomal DNA damage after radiation exposure: reply

We are grateful to Dr Yildiz and colleagues for their interest in our article. Their letter offers a unique opportunity to clarify several important points. First of all, it is important to focus on the physical dose–bio-dosimetric data correlation. In the original version of the manuscript, we indeed presented the data on the (lack of) correlation between Dose-Area Product and increase in micronuclei, but we were gently forced to delete them in the Revision process. As Reviewer 1 put it, ’no correlation between the radiation and the change in MN can be found due to the restricted sample size’, and therefore ’the issue should not be mentioned in any part of the manuscript’. And he was probably right! For any given dose, the amount of damage is modulated by several other factors: reactive oxygen species after coronary revascularization and levels of myocardial damage (as Dr Yildiz et al. nicely pointed out); amount of contrast (which sensitizes lymphocytes to radiation damage); environmental mutagens (such a smoking); and perhaps most importantly, polymorphism of genes involved in DNA damage and repair. That is why all the literature describes a weak, if any, correlation between physical dose and biodosimetric damage in the low dose range of acute and chronic exposures. We also agree that the increase of frequency of micronuclei in circulating lymphocytes would have been significant after coronary angiography with a larger sample size. But above and beyond these important statistical aspects, the challenge ahead is to identify the determinants of damage, eventually translating an estimate of population risk into an individually tailored radio-risk profile through biodosimetry. One might ask: Why to discuss these biodosimetric issues in a top cardiovascular journal? Cardiologists prescribe and/or practice >50% of all medical imaging examinations, accounting for about two-third of the total effective dose, which in US totals the dose equivalent of 160 chest x-rays per head per year to the average citizen. In April 2007, the American College of Radiology released the landmark ’White Paper on Radiation Dose in Medicine’, concluding that ’the expanding use of imaging modalities may result in an increased incidence of radiation-induced cancer in the not-too-distant future’. Cardiology is the epicentre of the radiological tsunami of the last 20 years, and the current cardiological practice is based on a deregulated, radiation-insensitive, and imaging prescription. Biodosimetry may help the scientist to shrink uncertainties still surrounding low dose effects and the clinicians to ‘see’, directly on their patients, the radiation damage through biomarkers of somatic DNA damage, which are intermediate endpoint of carcinogenesis and long-term predictors of cancer. Eventually, this will help the cardiologist to include the long-term risk in the risk-benefit balance, quintessential to determining the appropriateness of a diagnostic and therapeutic procedure, especially considering that more than one third of testing—even without considering radiation risk—are inappropriate in modern cardiology. It’s not radioprotection, it’s cardiology!

References


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Albuminuria and heart failure: is it an albuminuria or the hypertension?

Ingelsson et al. elegantly emphasized albuminuria as a risk factor for heart failure in elderly hypertensive men and present thought-provoking speculative mechanisms. However, the association between albuminuria and heart failure was seen in untreated hypertensive men compared to treated hypertension, suggesting that treated hypertensive men had advanced hypertension and thereby hypertensive heart disease with natural progression to heart failure, and therapy likely attenuated both the progression of albuminuria and heart failure. In the 40 untreated hypertensive men who developed heart failure, the amount of damage is modulated by several other factors: reactive oxygen species after coronary revascularization and levels of myocardial damage (as Dr Yildiz et al. nicely pointed out); amount of contrast (which sensitizes lymphocytes to radiation damage); environmental mutagens (such as smoking); and perhaps most importantly, polymorphism of genes involved in DNA damage and repair. That is why all the literature describes a weak, if any, correlation between physical dose and biodosimetric damage in the low dose range of acute and chronic exposures. We also agree that the increase of frequency of micronuclei in circulating lymphocytes would have been significant after coronary angiography with a larger sample size. But above and beyond these important statistical aspects, the challenge ahead is to identify the determinants of damage, eventually translating an estimate of population risk into an individually tailored radio-risk profile through biodosimetry. One might ask: Why to discuss these biodosimetric issues in a top cardiovascular journal? Cardiologists prescribe and/or practice >50% of all medical imaging examinations, accounting for about two-third of the total effective dose, which in US totals the dose equivalent of 160 chest x-rays per head per year to the average citizen. In April 2007, the American College of Radiology released the landmark ’White Paper on Radiation Dose in Medicine’, concluding that ’the expanding use of imaging modalities may result in an increased incidence of radiation-induced cancer in the not-too-distant future’. Cardiology is the epicentre of the radiological tsunami of the last 20 years, and the current cardiological practice is based on a deregulated, radiation-insensitive, and imaging prescription. Biodosimetry may help the scientist to shrink uncertainties still surrounding low dose effects and the clinicians to ‘see’, directly on their patients, the radiation damage through biomarkers of somatic DNA damage, which are intermediate endpoint of carcinogenesis and long-term predictors of cancer. Eventually, this will help the cardiologist to include the long-term risk in the risk-benefit balance, quintessential to determining the appropriateness of a diagnostic and therapeutic procedure, especially considering that more than one third of testing—even without considering radiation risk—are inappropriate in modern cardiology. It’s not radioprotection, it’s cardiology!

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Albuminuria and heart failure: is it an albuminuria or the hypertension?
failure during follow-up, the risk of heart failure was higher in those with higher degree of albumin excretion rate (AER). Authors presented analysis of various subgroups but I could not find a similar analysis in relation to the degree of hypertension. Urinary AER has been shown to be positively correlated with the degree of blood pressure.2–4 It is possible that men with higher elevations of blood pressure, in this untreated group had higher degree of AER. Hypertension per se is an important cause of heart failure. In this subgroup of untreated hypertensives, men with higher elevations of BP were at increased risk for both AER and heart failure. As the authors state that it is unlikely that a very small concentration of albumin in urine in itself is the cause of increased risk for heart failure. I agree with the conclusion that low-grade albuminuria is a marker for subclinical cardiovascular damage but cannot affirm from this study that it predisposes to future heart failure.

References

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Table 1 The association of urinary albumin excretion rate to heart failure incidence in participants without anti-hypertensive medication (n = 726)

<table>
<thead>
<tr>
<th>Model with hypertension (categorical)</th>
<th>Adjusted for hypertension (categorical) or systolic and diastolic blood pressure (continuous)</th>
<th>Adjusted for established risk factors for heart failure</th>
<th>Adjusted for established risk factors, C-reactive protein, clamp glucose disposal rate, NT-proBNP, and cystatin C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model with hypertension (categorical)</td>
<td>Hazard ratio for 1 SD increase in log UAER (95% CI)</td>
<td>P-value</td>
<td>Hazard ratio for 1 SD increase in log UAER (95% CI)</td>
</tr>
<tr>
<td>Model with systolic and diastolic blood pressure (continuous)</td>
<td>1.61 (1.30–2.00)</td>
<td>&lt;0.001</td>
<td>1.56 (1.21–2.03)</td>
</tr>
</tbody>
</table>

UAER, urinary albumin excretion rate; SD, standard deviation; CI, confidence intervals; NT-proBNP, N-terminal pro brain natriuretic peptide. Established risk factors for heart failure: Acute myocardial infarction before baseline, acute myocardial infarction during follow-up (modelled as a time-dependent covariate), diabetes, left ventricular hypertrophy, smoking, body mass index, and glomerular filtration rate estimated from creatinine.