Sex differences in outcome following community-based cardiopulmonary arrest

See page 239 for the article to which this Editorial refers

Today sudden death still represents a frequently observed event and a significant number of deaths are from cardiac causes. Among these latter, ischaemic cardiopathy is without any doubt the main, if not the only, cause of death, the quantity of variables, rendered reaching conclusions difficult. Kurkeiyan et al., for instance, on examining a series of 593 patients with acute infarction could be considered the cause of death, and the other in which no acute thrombosis can be observed and the cause of death is presumed to be chronic coronary artery disease.

With regard to the clinical presentation of the fatal event, very frequently a ventricular fibrillation, or a so-called shockable rhythm may be observed, but in several other instances, complete asystole is present, unresponsive to any electrical treatment. Finally, the symptomatology preceding sudden death might be important and last for hours, or days, while in other cases it could be non-existent, the fatal event being the first pathological manifestation in the patient.

In the many attempts to analyse gender as an independent factor in the determination of sudden death, the quantity of variables rendered reaching conclusions difficult. Kurkeiyan et al. for instance, on examining a series of 593 patients with acute infarction could be considered the cause of death, and the other in which no acute thrombosis can be observed and the cause of death is presumed to be chronic coronary artery disease.

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cardiopulmonary arrest found that 33% were women. The authors identified a cardiac pathology as cause of death in only 69% of the cases, whilst in 31% the event was due to other causes, such as pulmonary embolism, rupture of an aortic aneurysm, intracerebral haemorrhage, etc. Similarly, Leach et al.[3] in their series of 333 cases observed a prevalence of women in 31% of their cases, but in this series too, examined by autopsy, 38% of the events were not due to acute or chronic ischaemic pathology. In examining the prevalence of gender in sudden deaths reports, this clarification seems to be very important. In fact, rather than mix cases together, it may be useful to examine their various subgroups divided by pathology. For example, if we examine only patients who died suddenly because of certain ischaemic heart disease, no significant difference will be observed between the two genders with regard to the presence of acute thrombotic lesions responsible for sudden death[3].

The above underlines the great importance of having at one’s disposal, in this particular clinical setting, data from autopsy examinations. Unfortunately these are frequently not available in published reports. If the determination of sudden death is based only on clinical suspicion, more than one third of cases with a non-cardiac aetiology could be missed[2]. Kuisma and Alaspäät[2] suggest that the proportion of sudden death episodes of non-cardiac origin increases parallel to the increasing frequency of autopsies. Silfvast[4] has come to the same conclusion, showing that clinical suspicion alone is unreliable in the determination of the real cause of sudden death. This is particularly important when we try to interpret the electrophysiological mechanism underlying sudden death. We may hypothesize that the presence of a shockable rhythm is more easily attributable to an ischaemic pathology and that of asystole to a non-cardiac cause. Clear electrophysiological differences exist between men and women in the setting of a certain ischaemic pathology, with regard to the inducibility of sustained ventricular tachycardias in patients resuscitated from sudden death. Vaitkus et al.[5] demonstrated in such a population of patients (aborted sudden death in ischaemic heart disease) that a sustained ventricular tachycardia was inducible in 73% of males vs only 38% of females. This important difference was not justified by significant differences in ejection fraction, number of diseased coronary arteries or history of myocardial infarction.

These data clearly seem to suggest that factors other than substrate may be important in modulating the propensity to tachyarrhythmias, such as the role of the autonomic nervous system, the presence or absence of ischaemia, transient electrolyte imbalances. With regard to autonomic modulation Airaksinen et al.[6] have clearly shown gender related differences in autonomic responses to abrupt coronary occlusion, with a more common occurrence of bradycardic reactions and blood pressure lowering during the early stage of coronary occlusion in women than in men. Furthermore, women have a lower baroreflex sensitivity and a higher heart rate variability, characterized by a preponderance of high frequency compared to low frequency fluctuations[7].

Oestrogens might contribute to this effect, inhibiting the release of norepinephrine and increasing cholinomuscarinic activity in the heart, particularly under ischaemic conditions. This effect could result in an anti-brillatory action during acute myocardial ischaemia in women. Pell et al.[8] report in this issue on a large series of patients with out-of-hospital cardiopulmonary arrest in Scotland, addressing the possible differences in clinical presentation and outcome between males and females.

As reported in other studies, the women were significantly older than the men, had fewer shockable rhythms, collapsed more frequently at home than the men and were witnessed by bystanders. Women were more likely to survive hospital admission but thereafter were more likely to die in hospital.

The authors come to the conclusion that ‘women suffering cardiopulmonary arrest have a better early prognosis than men but that it represents only a postponement of death rather than avoidance’. Unfortunately, this work does not refer to autopsy data and therefore, besides the useful presentation of the large amount of data globally reported, very little can be obtained from it, to further clarify the real differences existing between men and women in the determination of cardiopulmonary arrest and its outcome.

In fact, it is now well known, from all the published series reporting cardiopulmonary arrests, that there is a large proportion of non-ischaemic pathology and a predominance of female sex in this subgroup. There are also important differences in autonomous nervous system modulation and in the high frequency of females among patients without shockable rhythms. Autopsy is therefore essential to allow definite conclusions. Without doubt, sudden death presents with many faces, many of which are still extremely obscure. Greater clarification is necessary before statements, particularly with regard to gender differences, can be made in this specific population of patients.

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Is the exercise test of use in post-menopausal women with unstable coronary artery disease?

See page 230 for the article to which this Editorial refers

The correct answer cannot be a simple ‘yes’ or ‘no’. The answer is a complex one. A first observation is that the exercise test has a very low predictive value for the presence of coronary artery disease in men as well as women in populations with a low incidence of coronary artery disease, for instance in pre-menopausal women or in men less than 40 years old[1]. Although the prevalence of coronary artery disease in women is lower than that in men, particularly in the pre-menopausal years, the prevalence of ST depression is higher in women younger than 45 years. This high prevalence of false-positive findings on exercise testing has been attributed to the presence of a higher oestrogen level. There is indeed good evidence that oestrogen may be a vasoconstrictor to coronary arterioles. It has a chemical structure similar to that of digitalis, which also has been demonstrated to be a vasoconstrictor. Men receiving large doses of oestrogen for carcinoma of the prostate have increased degrees of ST depression. It is, moreover, well known that because women have a lower prevalence of coronary artery disease than men, there are likely to be a higher number of false-positive tests with, as a consequence, a higher number of coronary angiograms performed in women for the diagnosis of coronary artery disease after a positive exercise test.

This bias in many studies will reduce the specificity, thus supporting the concept of false-positive tests in women. The true cause of the increased false-positive rate of exercise tests in women is nevertheless still being debated. In patients with a well documented history of coronary artery disease, as in patients after myocardial infarction or with angina pectoris, stable or unstable, ST segment depressions during exercise test or Holter monitoring are highly predictive of myocardial ischaemia[2]. Several authors have found that women with coronary artery disease have a frequency of myocardial ischaemia similar to that of men.

A second point is that women with coronary artery disease are more likely to have atypical symptoms, including the absence of chest pain at exercise; pain in other locations, such as the jaw, arms, shoulder, back, and epigastrium; and angina-equivalents, such as dyspnoea, palpitations, and pre-syncope. A safe and accurate approach for the detection of coronary artery disease in women must be guided by clinical likelihood based on patient age, chest-pain quality, and risk factors, mainly diabetes and post-menopausal status without hormone replacement therapy. Although computerized exercise ST-segment analysis and a multivariable approach for the interpretation of exercise tests were used, several authors have demonstrated that stress echocardiography is more sensitive than exercise score, and more sensitive and specific than ST-segment analysis for the diagnosis of coronary artery disease in women[3].

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