and doctor alike. It confirms the growing belief that the term syndrome X is no more than a flag of convenience encompassing a miscellany of heterogeneous conditions of differing pathogenesis. The current list includes impaired coronary flow reserve (microvascular angina), early cardiomyopathy, visceral sensory dysfunction, reduced efficiency of the potassium pump and insulin resistance. Chauhan et al. have now added a further subgroup in which the chest pain results from reduced coronary blood flow reflexly induced by oesophageal acid stimulation such as would occur with gastro-oesophageal reflux.

Importantly, this work has helped establish the existence of linked angina by providing a probable underlying mechanism i.e. the ability of oesophageal acid stimulation not only to cause anginal-type chest pain arising in its own pain receptors but also to induce true cardiac angina — at least in patients with syndrome X and possibly in those with coronary artery disease. Since cardiac and oesophageal disease commonly co-exist, clinicians should be aware that identical episodes of pain occurring at different times in the same patient may have entirely different origins. Consideration should, therefore, be given to simultaneous ambulatory ECG and pH monitoring or to well constructed therapeutic trials e.g. with omeprazole to distinguish cardiac from oesophageal episodes. In addition, treatment of both conditions may be necessary in order to render the patient symptom-free.

Increasingly, however, it does seem as though one route to a man’s (or woman’s) heart may be through the stomach!

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References


Spectral analysis of RR variability during transient myocardial ischaemia: have we moved from the computer console to the bedside?

See page 388 for the article to which this Editorial refers

While improvements in medical technology have rendered the clinical appreciation of the mechanical and metabolic effects of acute myocardial ischaemia a standard diagnostic procedure, the assessment of the attendant autonomic effects is still largely a matter of experimental investigation, which has not been resolved with simple determinations of plasma catecholamines.

Since the early observation that acute regional myocardial ischaemia in anaesthetized cats was capable of initiating a cardio-cardiac sympathetic excitatory reflex[1], the search for practical ways to address in the clinic the link between sympathetic
activity and ischaemic events has eluded investigators\textsuperscript{[2]}. In the context of transient myocardial ischaemia, increases in sympathetic activity may play multiple roles. An augmentation of sympathetic vasomotor tone could increase coronary artery resistance, reduce flow, and lead directly to either global or regional ischaemia. Sympathetic activation could strike the balance between O\textsubscript{2} supply and demand, through tachycardia, increase in arterial pressure or enhanced contractility (all important determinants of O\textsubscript{2} consumption). On the other hand, myocardial ischaemia could stimulate sensory endings, mostly in the ischaemic zone, by way of the abnormal mechanical behaviour of the ischaemic muscle or of the altered biochemical milieu and hence initiate cardiogenic reflexes.

The dual nature, vagal and sympathetic, of cardiac innervation accounts for the complexity of cardio-cardiac reflex responses, and requires specific models to be investigated. In conscious instrumented dogs\textsuperscript{[3]} cardiac sensory endings were stimulated chemically with small intracoronary injections of bradykinin, to mimic natural episodes of ischaemia. This stimulus induced a powerful excitatory autonomic reflex, that was characterized by increases in heart rate, arterial pressure and myocardial contractility, surprisingly in absence of signs of pain\textsuperscript{[3]}. These reflex excitatory responses were augmented by a prior vagotomy, highlighting a concurrent inhibitory interaction with the simultaneous activation of vagal mechanisms.

Finally, the combination of ischaemia and sympathetic overactivity represents a well known condition of enhanced vulnerability to severe arrhythmias and sudden death, that is, however, difficult to address directly in the clinical setting\textsuperscript{[2]}. The study of Vardas et al.\textsuperscript{[4]} in this issue suggests a more optimistic outlook regarding this latter important point. According to this study, spectral analysis of RR interval variability from standard Holter recordings could be used to describe the dynamics of the autonomic changes occurring with episodes of nocturnal ischaemia. In a well selected population of patients the authors report a clear time effect in the 10 min arbitrary window preceding the onset of ischaemia (assessed by ECG criteria): a reduction in the power of the high frequency, and an increase in the low frequency component. Accordingly, the LF/HF ratio presented a very strong increase before the ischaemic episodes. Concurrent increases in heart rate were observed, while (regrettably) no clear information on total heart rate variability was provided. The authors interpret their findings to indicate that, prior to the occurrence of ischaemia there is a gradual withdrawal of parasympathetic and a predominance of sympathetic tone.

The important aspect of the study is thus the demonstration that clinical episodes of transient ischaemia can be followed dynamically with this approach in the frequency domain, as has been previously shown with laboratory investigations in conscious dogs\textsuperscript{[5]}. Can we therefore assume that, from now on, spectral analysis of RR interval variability should be added to the cardiological diagnostic armamentarium? We might well be on the way, but not quite yet.

First of all, unresolved methodological issues still exist with data processing and presentation of results. For instance, Vardas et al.\textsuperscript{[4]} use absolute units, with a logarithmic transformation, to present values of individual spectral components, and also, the dimensionless LF/HF ratio. The use of absolute units (in ms\textsuperscript{2}) disregards the (mathematical) influence of total power (equivalent to variance or standard deviation squared) on the absolute power of individual components. Hence the uncritical comparison of the absolute powers of spectral components obtained in different conditions in which RR interval variance undergoes significant changes (because of such diverse factors as ageing, exercise, heart failure, acute myocardial ischaemia or diabetes, all of which reduce it; or sleep and beta adrenergic blockers, which increase it) may be affected by a large experimental bias.

However, the fractional distribution of power (which best codifies the balance between vagal and sympathetic modulatory nerve activity) can easily be appreciated with a simple normalization procedure\textsuperscript{[5]}, which handles both the possible bias of differences in variance, and the influence of the slow trends and non-stationarities, that frequently affect real life data, reducing the signal to noise ratio.

The use of specific algorithms (such as Fast Fourier Transform or AutoRegressive) is of minor concern, provided a reasonable length (200–500 beats, avoiding oversampling) and stationarity of the segment (without arrhythmias) is chosen for the analysis\textsuperscript{[6]}.

Recently a study addressing the question of the most efficient way to assess gradual changes in sympatho-vagal balance, modulating the sino-atrial node during autonomic changes produced by graded tilt, has indicated that both normalized units and the LF/HF ratio provide the most consistent results\textsuperscript{[6]}. Still undecided is the crucial question of the range of applicability of spectral analysis of RR variability, to infer neural control of the sino-atrial node. Great caution should be used when addressing conditions characterized by extreme tachycardia or very low
Non-invasive markers of coronary reperfusion in acute myocardial infarction

See page 399 for the article to which this Editorial refers

A sufficient number of controlled clinical trials have convincingly demonstrated that thrombolytic therapy reduces short-term and long-term mortality after acute myocardial infarction[1]. However, there are limitations to intravenous thrombolytic therapy. It has been shown that in approximately 30% to 35% of patients, intravenous thrombolysis fails to restore coronary artery patency[2]. Patients who fail to reperfuse do worse compared to patients with a patent infarct-related artery and furthermore there are also differences among reperfused arteries. For example, patients achieving an angiographic TIMI 3 score have a better outcome than those achieving only a TIMI 2 score.

Since different therapies are available to improve or to restore infarct-related coronary patency once thrombolysis has failed, and since time is usually a limiting and prognostic related factor, we are in need of reliable markers to determine whether successful reperfusion has occurred. Undoubtedly coronary angiography is the gold standard to determine reperfusion; however, for clinical practice it is impractical and not recommended. Non-invasive markers have been evaluated in order to distinguish between patients with successful and failed reperfusion and therefore to allow further treatment to those patients who failed to reperfuse following intravenous thrombolytic therapy.

Clinical symptoms (resolution of chest pain), electrocardiographic monitoring (reduction of ST segment elevation and appearance of accelerated idioventricular rhythm) and cardiac enzymes have all been used as non-invasive markers of reperfusion.

Shah et al.[3] conducted an angiographic validation study of bedside markers of reperfusion.