symptoms occurring during daily life are caused by vasoconstrictor stimuli stronger than ergonovine. The 20% of patients refractory to medical treatment in the study of Bory et al.\[4\] is somewhat higher than the 5–10% reported in previous studies\[6\]. The reasons for this discrepancy may lie in differences in patient populations or in treatment strategies. Surprisingly, Bory et al. did not treat their patients with intermittent long-acting oral nitrates which prevent smooth muscle contraction through a mechanism different to that of calcium antagonists and which therefore may help prevent coronary spasm in the period of the day in which it most often occurs. Furthermore, the maximal daily doses (360 mg for diltiazem, 480 mg for verapamil, 60 mg for nifedipine) of calcium antagonists given to their patients were lower than the maximal doses (960 mg for diltiazem and verapamil and 100 mg for nifedipine) given in previous studies, which also showed that the addition of guanethidine or clonidine to calcium antagonists and nitrates may offer further symptomatic relief, probably by a reduction of sympathetic vasoconstrictor stimuli\[6\].

Conclusions

In patients with coronary spasm and normal or nearly normal coronary arteries, the current treatment offers a relatively good prognosis, although symptom control can occasionally be difficult. Only understanding the causes of local non-specific hyperreactivity in coronary smooth muscle will enable new drugs to be designed specifically to treat coronary spasm. Drugs currently available, which reduce smooth muscle contraction in the whole body, are effective but exhibit frequent side effects; most importantly, in some patients, they may be unable to prevent a fatal episode of coronary spasm.

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References

seems attractive because chest pain in hypertrophic cardiomyopathy is often atypical, is not always initiated by exertion, and may be triggered by different factors during the day. For example, the magnitude of the pressure gradient may change dramatically during various daily situations. However, ambulatory ST monitoring in hypertrophic cardiomyopathy patients involves major technical problems. Previous Holter studies in normal subjects have shown occurrences of ST-depression in 5–30%, many recognizable as artifacts by careful analysis. However, patients with hypertrophy-determined resting electrocardiogram repolarization abnormalities were not considered eligible for such methodological analyses because the interpretation of ambulatory electrocardiogram findings is known to be very difficult. Even after exclusion of patients with left bundle branch block and persistent pacemaker rhythm or atrial arrhythmias, Elliott et al. in this issue, found that one-third of the remaining 94 patients evidenced ST-depression of ≥0.1 mV in the baseline 12-lead electrocardiogram and that a considerable number of additional patients showed only T wave changes. Moreover, it has not been investigated whether Holter results really add information to an exercise electrocardiogram, which may show ST-depression in a number of hypertrophic cardiomyopathy patients. Despite these limitations, the finding that transient ST-depression does not relate to a clinical history of chest pain and dyspnoea is new and important.

Elliott’s findings raise concern about the significance of perfusion defects in thallium-201 myocardial tomography. In agreement with other studies, Elliott et al. demonstrated the absence of a relationship between thallium abnormalities and subjective complaints. However, previous investigations show a close concordance with technetium-99m sestamibi, another perfusion agent, to abnormal lactate metabolism during rapid atrial pacing and an improvement by medication or a surgical reduction of the outflow gradient. These strongly support the hypothesis that thallium defects are related to myocardial ischaemia. These data suggest that both 'silent' and minor symptomatic ischaemia may play a relevant role in hypertrophic cardiomyopathy and/or that thallium-201 myocardial tomography may not be sensitive enough in all hypertrophic cardiomyopathy patients. In contrast to Elliott et al., there are some reports in which perfusion abnormalities, independent of clinical symptoms, indicated an adverse prognosis with a higher incidence of serious arrhythmias and sudden death. Some of these varying results may be explained by differences in methodologies and patient populations. Given the heterogeneity of the hypertrophic cardiomyopathy population with regard to anatomical, physiological and genetic characteristics, it follows that the causes of ischaemia and chest pain may differ completely from one individual to another. There are a number of potential mechanisms:

1. decreased coronary vasodilator reserve due to high diastolic pressure;
2. dysplastic small vessels, which may be present in hypertrophied and non-hypertrophied regions of the left ventricle, and cause increased vascular resistance and altered coronary reactivity;
3. inadequate capillary density due to extensive myocardial hypertrophy;
4. variable degrees of systolic reduction or inversion of coronary flow probably caused by compression of intramyocardial coronary vessels;
5. systolic compression of large vessels by myocardial bridges;
6. high oxygen demand in the presence of a large outflow tract gradient;
7. concomitant epicardial atherosclerotic disease; and
8. increased oxygen demand caused by episodes of sinus tachycardia or atrial arrhythmias.

Each diagnostic test may be more or less sensitive and specific in detecting various ischaemia subtypes. In this context, results of a recent investigation on dipyridamole echocardiography are remarkable because they revealed a surprising 100% specificity in identifying concomitant coronary artery disease in hypertrophic cardiomyopathy patients. Careful characterization of each patient may be essential for targeting the optimal therapeutic approach, including surgical or pharmaceutical options. For example, a high intracavitary pressure gradient and a high peak flow in the great cardiac vein during atrial pacing is predictive of symptomatic and metabolic improvement after surgical interventions. In contrast, patients with lower gradients or lower peak flows show little or no improvement; in the presence of angina, other mechanisms must be responsible, and drug therapy may be preferred. Of interest in the study of Elliott et al. is the correlation of chest pain and transient ST-depression in a subanalysis of patients under 30 years of age. Exertion dyspnoea was also more common in this subgroup. These data correspond to the results of Dilsizian et al., who found ST-depression during treadmill exercise more frequently among young hypertrophic cardiomyopathy patients with a history of syncope or cardiac arrest. Thallium investigations performed during the same exercise study revealed abnormalities in six additional patients. Elliott et al. did not attribute
any importance to thallium data even in these young patients. Nevertheless, it is open to speculation whether this important subgroup is characterized by a special anatomical substrate or pathophysiological mechanism leading to an extraordinarily high degree of subendocardial ischaemia.

Mainly because of methodological problems, ambulatory ST-monitoring seems to be of limited value for ischaemia screening in hypertrophic cardiomyopathy patients. One exception may be a subgroup of younger patients, but this still remains to be investigated. The ability of the various invasive and non-invasive hypertrophic cardiomyopathy diagnostics used to detect different mechanisms of ischaemia requires further clarification. Objective markers of ischaemia rather than chest pain or dyspnoea should be used to validate such strategies. Each individual hypertrophic cardiomyopathy patient might require the summation of several such tests to elucidate the ischaemia-triggering profile and to explain symptoms. Individual characterization of ischaemia or the division of the heterogeneous hypertrophic cardiomyopathy population into subgroups with similar mechanisms and anatomic substrates will be important to gain understanding of this complex issue.

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**References**


