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博士の専攻分野の名称	博士（医学）
学位記番号	第 16878 号
学位授与年月日	平成14年3月25日
学位授与の要件	学位規則第4条第1項該当 医学系研究科生体統合医学専攻
学位論文名	Exercise-induced stunning continues for at least one hour: Evaluation with quantitative gated single-photon emission tomography （運動負荷誘発スタニングには少なくとも1時間持続するものがある－定量的心電図同期SPETによる評価）
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論文内容の要旨

【Objective】

Increased oxygen demand during exercise in presence of coronary artery stenosis often results in myocardial ischemia and left ventricular(LV) dysfunction. Experimental studies have demonstrated persistent exercise-induced LV dysfunction beyond the resolution of ischemia as a manifestation of myocardial stunning. Nevertheless, substantial evidence of exercise-induced stunning in patients with coronary artery disease(CAD) remains elusive. ECG-gated myocardial single-photon emission tomography(SPET) offers the unique advantage of simultaneous assessments of LV perfusion and function within a single study. We aimed to elucidate whether LV contractile function in CAD patients, simultaneously evaluated with perfusion by ECG-gated myocardial SPET, remained impaired after the resolution of ischemic episode, as an evidence of exercise-induced stunning in CAD patients.

【Methods】

Fifty-three subjects with known or suspected CAD (mean age: 61±10 years) were studied. Patients with unstable angina, recent myocardial infarction, coronary revascularization, and arrhythmia were not considered. Each subject underwent symptom-limited bicycle exercise, and doses of technetium-99m tetrofosmin were injected at peakexercise and at rest according to a standard same-day exercise-rest protocol. Poststress and resting ECG-gated SPET images were acquired one-hour after injections of radiotracer using a triple-detector gamma camera. A validated quantitative program (Cedars-Sinai program) was applied to reconstructed short-axis data to quantitate LV end-diastolic volume (EDV), end-systolic volume(ESV), ejection fraction (LVEF) and systolic wall thickening (SWT). To minimize the effects of segmental heterogeneity, segmental wall thickening index (WTI), a ratio of SWT of a segment to that of a control segment(based on SWT of 10 healthy control subjects), was used as a measure of regional LV function. LV perfusion was assessed semiquantitatively on summed nongated tomograms. Reversibility score (RS), an index of severity of ischemia, was calculated as a difference in defect scores between exercise and rest.

【Results】

Subjects were classified on the basis of perfusion scan findings as follows: a normal group(n=16), who had no perfusion abnormalities, an ischemia group (n=19), who exhibited exercise-induced reversible perfusion abnormality, and an infarction group (n=18), who had only fixed perfusion abnormality.

In the normal group, poststress EDV, ESV and LVEF did not differ from resting values; the poststress WTI was similar to resting WTI in the normal segments (n=320). In the ischemia group, EDV (90±17ml) and ESV (44±15ml) one hour after exercise were significantly greater than EDY (84±15ml, P=0.001) and ESV (36±14ml; P<0.0005) at rest, respectively, and poststress LVEF was significantly depressed (53±9%vs 58±9% at rest, P<0.0001). The poststress WTI was impaired in the ischemic segments (n=82) compared to resting WTI (0.66±0.24 vs 0.78±0.24; P<0.0001), but were not different from resting value in the nonischemic segments (n=298, 0.91±0.47 vs 0.94±0.33). The difference in WTI between rest and poststress was significantly greater in the ischemic segments than in the nonischemic segments. Among the ischemic segments, intensity of ischemia was more severe in segments with poststress dysfunction (36/82; 44%) than those without (RS, 2.5±0.6 vs 1.2±0.5, P<0.0001). In the infarction group, only poststress ESV was higher than resting ESV; poststress and resting WTI were not different in both infarct (n=88) and noninfarct segments (n=272). Poststress LVEF was significantly lower than resting LVEF in 9 (47%) of the 19 ischemic patients, compared to none of the 16 normal subjects and 1 (<1%) of the 18 infarction patients. Poststress segmental dysfunction and global dysfunction was significantly correlated with the segmental RS (r=-0.78, P<0.0001) and summed RS (r=−0.92, P<0.0001), respectively. Since contractile abnormalities outlasted the ischemic episode(which usually, returns to baseline within 5-14 minutes) and eventually improved at resting acquisition, the poststress LV dysfunction in patients with ischemia observed in this study is consistent with the concept of exercise-induced stunning.

【Conclusion】

In conclusion, prolonged LV contractile dysfunction following exercise-induced ischemia, consistent with the 'myocardial stunning' does occur in CAD patients, and continues for at least one hour after exercise in severely ischemic patients. The magnitude of exercise-induced stunning is determined by the severity of ischemia induced by the exercise.

論文審査の結果の要旨

一過性虚血に伴う心筋収縮機能低下が心筋灌流回復後も持続する現象を myocardial stunning という。この概念は従来より実験的に証明されてきたが、今回の研究では運動負荷により誘発される虚血に基づく myocardial stunning の現象を、冠動脈疾患を有する患者を対象に臨床の場において証明することを目的とした。心筋灌流トレーサである^{99m}Tc-tetrofosmin を用いた心電図同期心筋 SPECT では運動負荷 1 時間後と安静時の両者において心筋灌流と同時に心機能を評価することが可能である。この同時評価という点でこの方法は他のモダリティーを卓越したものがあり、また global な機能と局所の機能をともに優れた定量性を持って客観的に評価することが可能である。本研究によって、正常心筋灌流の患者および虚血を伴わない心筋梗塞の患者では運動負荷 1 時間後と安静時の左室機能には差を認めなかったのに対し、運動により高度の虚血が誘発される場合、灌流が正常に復していても 1 時間後まで global な機能、局所機能ともに障害が持続していることを証明した。更に、その障害の程度は虚血の程度に左右されることを示した。

本研究において証明した運動負荷による虚血から生ずる遷延する左室機能障害は myocardial stunning の概念に一致し、臨床的に虚血を繰り返す冠動脈疾患患者における左室機能障害および心不全発生の機序解明に重要と考えら

れる。更にその心筋虚血の程度がいかに重要であるかを示し、このような患者に対する薬物療法を考えるうえで非常に参考となる研究であると見なされる。また、この研究において、心電図同期SPECTでは運動負荷1時間後であっても、必ずしも運動時心筋血流と安静時機能を評価しているわけではなく、虚血の厳しい場合はstunningの現象を捉えている可能性を考慮すべきであることが確認された。

このように本研究は、虚血性心疾患患者における臨床に関する大変重要な概念を証明したため、学位論文として十分な価値があると認められる。