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^{99m}Tc-MIBI muscle imaging and approach to assess functional anatomy of lower limb muscles

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ABSTRACT: ^{99m}Tc hexakis-2-methoxyisobutyl-isonitrile (^{99m}Tc-MIBI) has been seldom used as a skeletal muscle tracer, and exercise changes of radionuclide uptake in different muscle groups have not been explored. The image pattern of ^{99m}Tc-MIBI uptake in the lower extremities was studied in 15 subjects (14 men, one woman; mean age: 59.9 ± 12.6 years) with no evidence of muscle or peripheral vascular disease, both at rest and during treadmill exercise. Several muscles could be identified in the scanned regions. No association was found between the intensity of uptake and some cardiovascular and metabolic parameters, but as a whole exercise increased radionuclide uptake in the calves. ^{99m}Tc-MIBI scintigraphic imaging might be a useful technique to assess the functional anatomy of lower limb muscles.

Introduction

^{99m}Tc hexakis-2-methoxyisobutyl isonitrile (^{99m}Tc-MIBI) is a radiopharmaceutical which has been widely used for in vivo imaging of myocardial perfusion [1,2] and, less frequently, for evaluation of tumor processes[3,4]. ^{99m}Tc-MIBI is a lipophilic cation that behaves like Na+ and uses the Na+/H+ antiport system to enter the heart cell [5]. It eventually goes through the outer and inner membranes of mitochondria, and accumulates into the mitochondrial matrix [6] by a mechanism that largely depends on the transmembrane potential [7]. As might be expected, this radiotracer settles not only in the myocardium, but also in skeletal muscles.

A few studies have investigated the potential role of skeletal muscle imaging with ^{99m}Tc-MIBI in the assessment of peripheral vascular disease [8-13], compartment syndrome [14], uremic [15] and statin induced [16] myopathies, systemic sclerosis [17], Duchenne muscular dystrophy [18], and the paralytic phase of thyrotoxic periodic paralysis [19]. Muscular response to propionyl-L-carnitine [20] and neuromuscular electrical stimulation [21] has also been explored with this imaging technique. However, no one of these studies has focused on the muscular response to exercise and the feasibility to depict muscular anatomy. Besides, technical limitations of former devices -i.e. insufficient spatial resolution- might have restricted the use of ^{99m}Tc-MIBI as a skeletal muscle tracer. In the present study, we test: 1) whether muscular morphological data can be obtained from ^{99m}Tc-MIBI scintigraphic images, and 2) the association between ^{99m}c-MIBI muscular uptake and some physiological parameters obtained during exercise.

Materials and methods

Subjects

Fifteen patients (14 men, one woman; mean age: 59.9 ± 12.6 years, range: 26 to 77 years) were included. They had been sent to the nuclear medicine department for myocardial single photon emission computed tomographic (SPECT) study with ^{99m}Tc-MIBI in order to discard ischemic heart disease. None of the subjects had any complaints referred to the lower extremities. Specifically, they did not show any clinical evidence of either peripheral vascular disease or muscle disease. Those patients who had any systemic disease that could affect muscular metabolism, such as diabetes mellitus, were excluded. Subclinical or masked effects of cardiovascular disease in the lower extremities could not be ruled out, but they would have not changed the validity of our study as for the established purposes.

The study protocol was approved by the local ethical committee, and written informed consent was given by all the patients. Radiopharmaceutical and imaging protocol.

Each patient underwent a two days protocol for scintigraphic study of ischemic heart disease. The details can be found elsewhere [22]. Briefly, conventional rest and post stress (treadmill exercise) SPECT studies were acquired after an intravenous administration of 740-925 MBq of ^{99m}Tc-MIBI (Cardiolite®, Bristol-Myers Pharma, Brussels, Belgium) prepared according to the manufacturer's instructions. Ten minutes after conventional myocardial tomographic studies, planar images were obtained from the lower extremities with a dual head whole-body gamma camera (DST-Xli, Sopha Medical Vision International, Buc, France) equipped with a low-energy high-resolution collimator. Anterior and posterior images of thighs and calves were obtained for 5 minutes in 256 x 256 pixel matrices, with the pixel width being 2.1 mm. Close to the surface of the patient, theoretical intrinsic spatial resolution (RI) was 3.5 mm and collimator spatial resolution (RC) was 2.5 mm. Overall system resolution (RS) is given by the formula [23]

$$R_S = \sqrt{R_C^2 + R_I^2}$$

and it equals 4.3 mm.

Image analysis and interpretation

Visual evaluation was performed comparing scintigraphic images with corresponding pictures on a standard atlas of human anatomy [24], and muscles were depicted according to them. Images were evaluated by both a neurologist (MLC) and a specialist in nuclear medicine (JAA), and a consensus on anatomical correspondence was reached. To assess muscular activity, rectangular regions of interest that comprised the whole thigh over the anterior view and the whole calf over the posterior view were drawn on each side. Mean counts per pixel within the selected regions were calculated. Since no significant difference was found between right and left activities, data for further analysis were derived from the average of right and left values. Knee areas without muscular tissue were taken as control, and results were expressed semiquantitatively as the percentage of uptake with respect to the uptake in the knees.

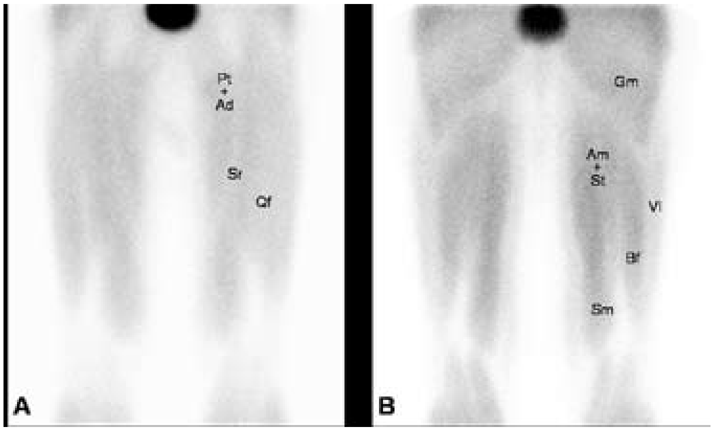

Figure 1. 99mTc-MIBI muscle scintigraphy obtained from a 55 year-old man after treadmill exercise. (A) Anterior view of the thighs: Pt+Ad, pectineus and adductors (superimposed); Sr, sartorius; Qf, quadriceps femoris. (B) Posterior view of the thighs: Gm, glutaeus maximus; Am+St, adductor magnus and semitendinosus (superimposed); Sm, semimembranosus; Bf, biceps femoris; Vl, vastus lateralis of quadriceps femoris.

Other clinical measurements

Body weight and height of all the patients were registered at the time of assessment. In addition, maximum systolic blood pressure, maximum heart rate, and oxygen comsumption as the metabolic equivalent of the task (MET) were measured during exercise.

Statistical analysis

For each region of interest, values of uptake at rest and exercise were compared making use of the one-tailed paired Student's t-test. Correlation between variables was analyzed by means of the Pearson coefficient.

Results

Though superimposed muscles contributed to planar images, the following individual muscles and/or muscular groups could be identified in all the patients: 1) in the thighs (Fig. 1), adductors, sartorius, quadriceps femoris, glutaeus maximus, semitendinosus, semimembranosus, and biceps femoris, and 2) in the calves (Fig. 2), tibialis anterior, and triceps surae, with the two heads of gastrocnemius and the belly of soleus being recognizable.

From a qualitative point of view, the muscles were more visibly depicted after exercise, specially in the calves. From a quantitative point of view, muscle exercise significantly increased ^{99m}Tc-sestamibi uptake with respect to rest uptake in the calves (210.3 % vs. 185.2 %, $p<0.01$), but not in the thighs (265.8 % vs. 267.8 %, n.s.). Otherwise, no correlation was found between the intensity of uptake and any of the clinical measurements that were taken during exercise testing.

Discussion

^{99m}Tc-MIBI is generally used to evaluate myocardial perfusion or tumor activity, but it has also proved to be an adequate tracer for skeletal muscle. Some technical limitations might have restricted the use of ^{99m}Tc-MIBI muscle scintigraphy with former devices, but current equipment has allowed us to get rather sharp images of skeletal muscles. Moreover, ^{99m}Tc-MIBI muscle imaging could be further improved by increasing the time of acquisition of planar images or by getting tomographic images with SPECT.

We have made use of ^{99m}Tc-MIBI muscle scintigraphy in a group of patients who were free of muscle disease. In this setting, ^{99m}Tc-MIBI has provided us with anatomical information, as major muscle groups and even some individual muscles could be located on scintigraphic images. In addition, it has given some functional information, as there was a qualitative and quantitative change of ^{99m}Tc-MIBI uptake during exercise. The muscles that showed a significant increase of uptake were those most implicated in walking and running, i.e. the muscles of the calves [25]. Presumably the effects of muscle activity on ^{99m}Tc-MIBI uptake would have been different with another type of exercise. On the other hand, even with running the analysis of smaller regions of interest restricted to individual muscles might have shown an increase of uptake in additional locations.

To date, muscle imaging with ^{99m}Tc-MIBI has focused mainly on the vascular properties of this tracer [8-13], but only marginal attention has been paid to the possibility of tracing muscular disorders [17-19]. Furthermore, the effect of muscle activity on ^{99m}Tc-MIBI scintigraphy has not been thoroughly investigated for clinical purposes. Due to the pharmacokinetical properties of ^{99m}Tc-MIBI, this technique might be particularly suitable for the assessment of mitochondrial diseases. In fact, a cardiac decrease of ^{99m}Tc-MIBI-uptake has already been demonstrated when the heart is involved in some mitochondrial gene abnormalities [26-28]. It would be worth exploring any potential applications of rest and exercise ^{99m}Tc-MIBI imaging in the evaluation of different myopathies.

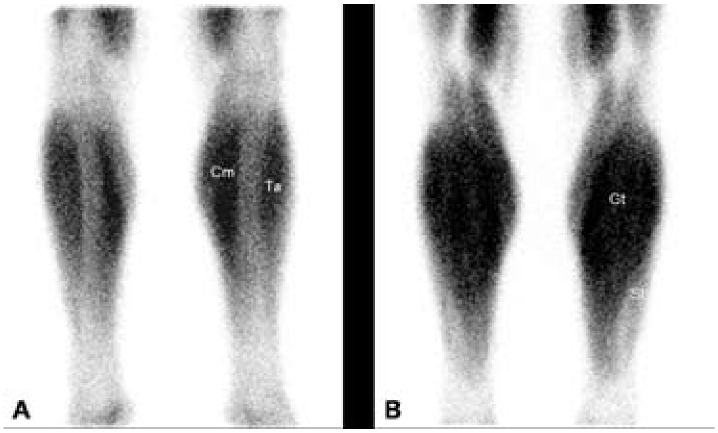

Figure 2. ^{99m}Tc-MIBI muscle scintigraphy obtained from a 55 year-old man after treadmill exercise. (A) Anterior view of the thighs: Ta, tibialis anterior; Cm, caput mediale of gastrocnemius. (B) Posterior view of the calves: Gt, gastrocnemius (caput mediale and caput laterale); Sl, soleus.

^{99m}Tc-MIBI scintigraphic imaging might be a useful technique to assess the functional anatomy of skeletal muscles in both health and disease conditions. Undoubtedly, this technique cannot compete with positron emission tomography (PET) as the gold standard in metabolic imaging [29-33]. However, it offers some advantages over PET: 1) the procedure is more simple; 2) it has much lower cost, and 3) it provides different metabolic information, since ^{99m}Tc-MIBI is a mitochondrial tracer and does not follow the route of 18F-fluoro-deoxy-glucose, i.e. the usual tracer in PET.

Conclusion

^{99m}Tc-MIBI scintigraphic imaging is a simple procedure that provides both anatomical and functional information about skeletal muscles. Further research is needed to ascertain any potential clinical applications of ^{99m}Tc-MIBI for tracing muscular disorders.

Abbreviations

MBq: megabecquerel
PET: positron emission tomography
SPECT: single photon emission computed tomography
^{99m}Tc-MIBI: ^{99m}Tc hexakis-2-methoxyisobutyl isonitrile
RI: intrinsic spatial resolution
RC: collimator spatial resolution
RS: overall system resolution

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