Comparison of cyclic RGD peptides for \(\alpha_v\beta_3\) integrin detection in a rat model of myocardial infarction.

Expression of \(\alpha_v\beta_3\) integrin is increased after myocardial infarction as part of the repair process. Increased expression of \(\alpha_v\beta_3\) has been shown by molecular imaging with \(18F\)-galacto-RGD in a rat model. The \(68Ga\)-labelled RGD compounds \(68Ga\)-NODAGA-RGD and \(68Ga\)-TRAP(RGD)3 have high specificity and affinity, and may therefore serve as alternatives of \(18F\)-galacto-RGD for integrin imaging. Left coronary artery ligation was performed in rats. After 1 week, rats were imaged with \([13N]NH_3\), followed by \(18F\)-galacto-RGD, \(68Ga\)-NODAGA-RGD or \(68Ga\)-TRAP(RGD)3 using a dedicated animal PET/CT device. Rats were killed, and the activity in tissues was measured by gamma counting. The heart was sectioned for autoradiography and histology. Immunohistochemistry was performed on consecutive sections using CD31 for the endothelial cells and CD61 for \(\beta_3\) expression (as part of the \(\alpha_v\beta_3\) receptor). In vivo imaging showed focal RGD uptake in the hypoperfused area of infarcted myocardium as defined with \([13N]NH_3\) scan. In autoradiography images, augmented uptake of all RGD tracers was observed within the infarct area as verified by the HE staining. The tracer uptake ratios (infarct vs. remote) were 4.7 ± 0.8 for \(18F\)-galacto-RGD, 5.2 ± 0.8 for \(68Ga\)-NODAGA-RGD, and 4.1 ± 0.7 for \(68Ga\)-TRAP(RGD)3. The
68Ga-NODAGA-RGD ratio was higher compared to 68Ga-TRAP(RGD)3 (p = 0.04), but neither of the 68Ga tracers differed from 18F-galacto-RGD (p > 0.05). The area of augmented 68Ga-RGD uptake was associated with ?3 integrin expression (CD61). 68Ga-NODAGA-RGD and 68Ga-TRAP(RGD)3 uptake was equally increased in the infarct area at 1 week post infarction as 18F-galacto-RGD. These results show the potential of 68Ga-labelled RGD peptides to monitor integrin expression as a part of myocardial repair and angiogenesis after ischaemic injury in vivo.

Zeitschriftentitel / Abkürzung:
EJNMMI Res

Jahr:
2013

Band:
3

Heft / Issue:
1

Seiten:
38

Sprache:
ing

Pubmed:

TUM Einrichtung:
Nuklearmedizinische Klinik und Poliklinik; Institut für Allgemeine Pathologie und pathologische Anatomie

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