題名:Granulocyte colony-stimulating factor increases sympathetic reinnervation and the arrhythmogenic response to programmed electrical stimulation after myocardial infarction in rats.

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摘要:Granulocyte colony-stimulating factor (G-CSF) has been used for the repair of infarcted myocardium, but concerns have been raised regarding its proarrhythmic potential. We analyzed the influence of G-CSF treatment on sympathetic nerve remodeling and the expression of nestin in a rat model of experimental myocardial infarction (MI). Twenty-four hours after ligation of the anterior descending artery, male Wistar rats were randomized to receive either saline (MI/C) or G-CSF (MI/G) for 5 days. At 56 days after infarction, MI/G rats had a significantly higher left ventricular ejection fraction accompanied by a significant decrease in the left ventricular end-diastolic dimension than the MI/C group. Myocardial norepinephrine levels revealed a significant elevation in MI/G rats in the border zone compared with MI/C rats. Immunohistochemical analysis for tyrosine hydroxylase, growth-associated protein 43, and neurofilament also confirmed the changes of myocardial norepinephrine. At 5 days after infarction, MI/G rats had increased numbers of tissue-infiltrated CD34(+) cells, although a similar increase in circulating neutrophil counts between sham-operated rats treated with G-CSF and MI/G rats was observed. Compared with MI/C rats, MI/G rats showed an increase of nestin and nerve growth factor expression, as assessed by protein expression and mRNA levels. The arrhythmia scores during programmed stimulation were significantly higher in MI/G rats than in MI/C rats, suggesting proarrhythmic potential. These findings suggest that,

although G-CSF administration after infarction improved myocardial function, it resulted in the activation of nestin and nerve growth factor expression and increased sympathetic reinnervation, which may increase the arrhythmogenic response to programmed electrical stimulation.