심근 섬유증의 유형 및 밀도가 심실 펌핑 성능에 미치는 영향의 규명을 위한 전산 연구

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Computational study to investigate the influence of myocardial fibrosis types and density on ventricular pumping performance

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Abstract : The presence of increased fibrotic myocardial tissue is strongly correlated to the induction of arrhythmias and may lead to sudden cardiac death in extreme cases. Studies showed that it is not only fibrosis amount but spatial distribution of fibrotic tissue also plays a major role in aggravating the arrhythmogenecity effect. In this study, we compared the influence of different fibrosis types and fibrosis amounts on the arrhythmogenesis of ventricles. In addition, the effect of fibrosis on pumping capacity of ventricles was investigated. Diffuse, patchy and compact fibrosis types with fibrosis amount 10, 30, 50 percent were generated. We observed that ventricular arrhythmogenecity depends on the amount of fibrosis amount in simulations involving diffuse fibrosis amount while in both compact and patchy fibrosis forms, it depends on the spatial distribution of the fibrotic tissue. Left ventricle mean stroke volume reduced as the fibrosis amount increased in all fibrosis types. ATP consumption rate was also linearly dropped as fibrosis amount increased, predisposing to the ventricles contractility impairment. In conclusion, fibrosis pattern is more crucial than fibrosis amount for sustaining and aggravating ventricular arrhythmogenesis.

1. 서 론

Cardiac fibrosis is an integral component of nearly all forms of cardiac arrhythmias [1]. It alters the architecture of the myocardium [2] and disrupts the coordination of myocardial excitation-contraction coupling in both systole and diastole and may result in profound systolic and diastolic dysfunction [3]. Studies reported that arrhythmogenecity of ventricles is highly correlated with the amount of fibrosis in the myocardium [1]. Moreover, clinical studies furthermore suggest that it is not only the fibrosis amount but spatial distribution of fibrosis also aggravate the arrhythmogenecity effect [4, 5].

In this study, we investigated influence of fibrosis amount and fibrosis pattern in electrical instablility of ventriclces. For that, we generated diffuse, compact and patchy fibrosis types with 10, 30 and 50 percent fibrosis amounts each. In addition, we studied how the different fibrosis patterns and fibrosis densities compromise the pumping efficacy of the ventricles.

2. 본 론

We employed Ten Tussher [6] model to simulate the ventricular cardiomyocyte behavior. The regional electrophysiological changes due to fibrosis is represented by 50% reduction in inward rectifier potassium current (I_{Ks}); 50% reduction in L-type calcium current (I_{CaL}); and 40% reduction in sodium current (I_{Na}). Furthermore, conductivity values in fibrotic regions were reduced by 30% to mimic the conduction delay due to fibrosis [7,8].

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To asses the effect of fibrosis amount and spatial distribution, we conducted 3D electrophysiological simulation under reentry condition with BCL of 600 ms and the we extracted the transient Ca^{2+} information. The extracted Ca^{2+} information was used to the mechanical simulation to mimic the cardiac excitation contraction coupling.

2.1. Arrhythmogenesis of fibrosis

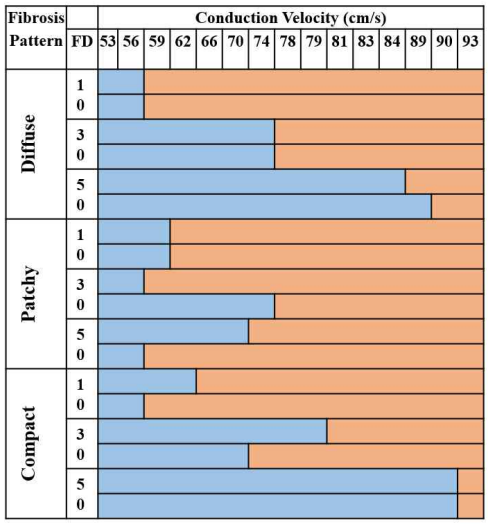

Table. 1 Arrhythmogenesis comparison between diffuse, patchy and compact fibrosis types. Blue and regions indicate conduction velocity ranges during which the triggered reentrant wave sustained to the end of simulation time and failed to sustain respectively.

2.2. Mechanical Responses

Parameter	Mean stroke volume			Mean Peak Pressure			ATP CR (s^{-1})		
FD	10	30	50	10	30	50	10	30	50
Diffuse	0.76	1.75	1.35	42.4	35.1	31.9	559	484	395
	5.1	2.6	0.75	40.3	32.9	36.8	565	497	394
Patchy	4.25	1.38	0.9	46.8	30.4	29.2	560	462	362
	1.2	1	0.82	31.6	35.6	32	562	474	367
Compact	1.6	0.85	0.6	36.5	30.2	32.3	560	451	354
	1.35	1.16	1	35.4	29.6	26	547	441	359

Table. 2 Mechanical responses. Mean left ventricle (LV) stroke volume, mean LV peak pressure and ATP consumption rate.

3. 결 론

Various fibrosis patterns and spatital fibrosis distributions yet with the same amount of fibrosis have different level of arrhythmogenecity. Hence, spatial fibrosis distribution has a major role in inducing and perpetuating arrhythmias.

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