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PROLONGED VENTRICULAR CONDUCTION TIMES AND FIBROSIS IN SENESCENT HEARTS WITH SELECTIVELY INCREASED LATE SODIUM CURRENT

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doi:10.1136/heartjnl-2013-304019.230

Background It has been postulated that increased late sodium current could contribute to structural abnormalities in the heart. To better delineate the contribution of an increased late sodium current to the ageing heart, we studied a knock-in murine model with exclusive increase of the late sodium current (deletion of KPQ in Scn5a gene, dKPQ.

Methods Interventricular activation times from isolated murine hearts aged 2 months to 2 years were measured from monophasic action potentials during endocardial right ventricular pacing at 100ms fixed-rate cycle length. For histology, 4 μm-thick sections of paraffin-embedded hearts were stained with picrosirius red/haematoxylin. Fibrosis was expressed as % of connective tissue relative to total tissue inside the region of interest. RT-PCR was carried out using SYBR-green and the ΔΔCt method.

Results Conduction times were longer in middle aged and senescent dKPQ mice (2–5 months: 11±1, vs. 13±1ms; 6–9 months: 10 ±1 vs. 16±1ms*; 18–24 months: 13±1 vs. 17±1ms*, n=7–11 per group, mean±SEM, *p< 0.05 vs. WT. Consistent with the subtle conduction time delay, there was subtle ventricular fibrosis in old dKPQ hearts and upregulation of several genes involved in fibrosis, compared with old WT hearts. Fibrotic area in senescent hearts encompassed 4±1% of LV tissue in dKPQ compared with 1±1% in WT*.

Conclusion A selective increase of the late sodium current may adversely affect ventricular activation chronically, and this may be linked with ventricular fibrosis.