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Myocardial gap junction channel protein, connexin-43, most likely modulates susceptibility of the heart to lethal arrhythmias.

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Functional electrical and metabolic cell-to-cell communication via gap junction connexin (Cx) channels ensures myocardial synchronisation while defects in Cx expression and/or distribution are thought to be arrhythmogenic facilitating occurrence of lethal arrhythmias. We examined topology and expression of myocardial Cx43 as well as susceptibility of the isolated working heart to ventricular fibrillation (VF) in hypertensive, hyperthyroid and diabetic (type 1) rats and diabetic rats treated with thyroid hormone and compared to healthy rats. All diseased hearts exhibited myocardial Cx43 remodelling that was most pronounced in hypertensive rats. Total Cx43 and its phosphorylated forms were significantly decreased in hypertensive and hyperthyroid while increased in diabetic rat hearts comparing to controls. However, treatment of diabetic rats with thyroid hormone suppressed both expression and phosphorylation of Cx43. Hypertensive and hyperthyroid rats were much prone to develop VF compared to healthy controls unlike diabetic rats that were much less. However, treatment of diabetic rats with thyroid hormone increased their vulnerability to VF. These findings indicate that Cx43 is most likely involved in modulation of cardiac susceptibility to malignant arrhythmias, i.e. up-regulation of Cx43 is associated with decrease while down-regulation with increased vulnerability. Further studies are needed to examine whether currently used cardio-protective drugs exhibiting antiarrhythmic potential (statins, ACEI, sartans) affect Cx43 expression and/or distribution.