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• 研究人員	謝敏雄 Hsieh, Ming-Hsiung
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• 中文摘要	背景：心房顫動及心臟衰竭是兩種非常常見的心血管疾病，許多臨床及動物實驗皆顯示心臟衰竭會導致心房擴大、心房纖維化、及心房凋零，這些心房結構的變化導致心房顫動的產生。此外，心房的再塑作用可能是導致心房顫動引發及持續的原因，這包括細胞性、結構性及電氣性再塑。然而心臟衰竭後整個心房的電量圖改變則仍未有報導。另外，心肌細胞間隙連結(包含連結素 40 及 43 及 annexin-6)的分布、大小、及數量會影響心房的電氣傳導，以前的研究也顯示間隙連結再塑作用在心房的再塑作用及心房顫動的引發及持續扮演極重要的角色，然而心臟衰竭引起心房的間隙連結再塑作用仍是未明。因此本實驗主要在探究心臟衰竭後心房之組織病理特性。方法：我們在非接觸式立體定位系統偵測下，12 隻正常成狗及 12 隻心臟衰竭成狗分別將心臟取出，再接上蘭根道夫(Langendorff)模式，之後接受不同部位電刺激，記錄右心房組織電位變化，並藉由立體定位標誌電位較高及電位較低之心房組織，電生理檢查完成後將心臟自狗取出，進行組織採樣。最後使用組織顯微鏡檢、定量免疫標定與西方墨點標誌分析對不同細胞標記的分布與表現進行分析。結果：心電生理特性中心臟衰竭狗與正常狗相近，但心房顫動引發的機率及維持心房顫動的時間皆較正常狗來得高。在光學顯微鏡下，右心房組織心肌層厚度兩組近似，但心衰竭狗有較明顯之纖維化增生。免疫共軛組織研究中，以不同切片部位連結素染色點分布總面積與總數之變異係數來評估連結素分布離散程度，其中心臟衰竭狗之連結素 43 分布，在分布總面積與分布總數上，其變異係數值均明顯高於正常狗;而連結素 40 分布在兩組則無多大差異。西方墨點蛋白質分析中，心衰竭狗之右心房連結素 43 明顯低於正常狗，但連結素 40 則兩組相近。結論：在心臟衰竭狗之心房電生理特性明顯比正常狗容易產生心房顫動，同時連結素 43 在心臟衰竭狗之右心房呈現不均勻分布，此等性質可能與心房不均勻的傳導特性與心房顫動的持續有關。

- 英文摘要

Atrial fibrillation and heart failure are two very common cardiovascular disorders. Clinical and experimental studies have demonstrated that atrial dilatation with atrial fibrosis or apoptosis is considered as the structural changes of heart failure to develop atrial fibrillation. In addition, previous studies have demonstrated that atrial remodeling, including cellular, structural and electrical remodeling, may be responsible for the initiation and maintenance of atrial fibrillation. However, the voltage changes of atrial substrate in heart failure have not been defined. On the other hand, the distribution, size and amount of gas junctions (consist of connexin 40 and 43) in the cardiomyocytes may influence the electrical conduction properties of atria. Previous studies also demonstrated that gap junctional remodeling may play an important role of atrial remodeling and the maintenance of atrial fibrillation. However, the atrial gap junctional remodeling in heart failure remains unclear. Therefore, the first step of our study was to investigate the immunohistopathological characteristics of different conduting substrates. Methods：Under the guidance of noncontact mapping system, 12 adult normal and HF dogs received electric stimulation from different sites in different coupling intervals. AF was induced from multiple pacing sites and the duration of induced AF was determined. After noncontact mapping, 8 to 10 pieces of atrial tissues were sampled from different sites of RA for analysis of gap junctions, including connexin43 (Cx43) and 40 (Cx40). Results：In the electrophysiological properties, the 12 HF dogs had similar properties to the 12 control dogs in four different atrial sites. However, the HF dogs had a higher AF inducibility and longer duration of AF paroxysms than normal dogs. In the light microscopy, the average thickness of RAmyocardial layers were similar in both HF and control dogs. In the immunoconfocal studies, the coefficient of variation (COV, standard deviation／mean X100%) of the total areas and numbers of immunolabeled Cx43 and Cx40 dots from at least 5 different views of each piece of tissue were determined. In HF dogs, the COV of total areas and numbers of Cx43 were significantly higher compared to normal dogs. InWestern blot protein analysis, the total Cx43 protein levels were reduced in HF dogs than in control dogs, while the total Cx40 levels remained similar in both groups. Conclusions: HF dogs had heterogeneous expression and down regulation of gap junction protein in the RA, which might relate to the heterogeneous conduction properties and contribute to the maintenance of AF.