低酸素負荷後の再酸素化で起こる心収縮力回復を改善するコエンザイムQ_{10}の可能性ある機序.

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Possible Mechanism by Which Coenzyme Q_{10} Improves Reoxygenation–Induced Recovery of Cardiac Contractile Force after Hypoxia

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ABSTRACT: To elucidate possible mechanisms by which coenzyme Q_{10} enhances reoxygenation–induced recovery of cardiac contractile foorce after hypoxia, rabbit hearts were subjected to hypoxic perfusion for 20 min, followed by 45 min–reoxygenation with or without pretreatment with coenzyme Q_{10}. Hypoxia induced a decline in cardiac contractile force, a decrease in myocardial high–energy phosphates and a release of ATP metabolites and creatine phosphokinase from the perfused hert. Upon reoxygenation the rate of release of ATP metabolites subsided, but no appreciable recovery of the loss of contractile force and the reduction of myocardial ATP content was seen, and the release of creatine phosphokinase was increased further. Pretreatment of rabbits with coenzyme Q_{10} resulted in an appreciable recovery of cardiac contractile force and of myocardial ATP content upon reoxygenation. The release of creatine phosphokinase from hearts during hypoxia and reoxygenation was inhibited completely by the pretreatment. Changes in the UV absorbance of the perfusate suggested that coenzyme Q_{10} reduced the loss of ATP metabolites from hypoxic hearts. Furthermore, high–performance liquid chromatographic analysis indicated that coenzyme Q_{10} attenuated the release of inosine and hypoxanthine from the hearts and decreased myocardial inosine and adenosine content of the hypoxic heart, suggesting that coenzyme Q_{10} retards the breakdown of ATP metabolites which are possible substrates for a salvage synthesis of ATP, when oxygen is replenished. This could account for an appreciable restoration of ATP, and eventually provide a significant recovery of cardiac contractile force upon reoxygenation.

抄録　低酸素負荷後の再酸素化で起こる心収縮力回復を改善するコエンザイムQ$_{10}$の作用機序を明らかにするためにコエンザイムQ$_{10}$処置後家兎心臓を摘出し，20分低酸素負荷後，45分再酸素化した。低酸素化は心収縮力低下，高エネルギーリン酸化合物減少，心臓からのＡＴＰ代謝物とクレアチンキナーゼの遊離をひき起こした。再酸素化でＡＴＰ代謝物遊離は抑制された。心収縮力の消失回復やＡＴＰ量の回復は観察されなかった。クレアチンキナーゼ遊離はむしろ増大した。コエンザイムQ$_{10}$前処置で再酸素化による心収縮力回復は認められ，心筋ＡＴＰ量は回復した。薬物処置でクレアチンキナーゼ遊離は抑制され、ＡＴＰ代謝物の遊離も抑制された。ＨＰＣＬ分析で心筋からのＡＴＰ代謝産物の遊離阻止と低酸素化心のＡＴＰ代謝産物量の減少が観察された。このことはＡＴＰ代謝物分解を遅らせ，これがＡＴＰサルベージ合成の基質となる可能性を示唆した。これが心収縮力回復につながると考えられる。