RECENT HIGH-IMPACT PAPERS FROM RADBOUDUMC RESEARCHERS

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With over 3,000 publications each year, scientific research is a cornerstone of the Radboud university medical center [1]. In this section, recent high-impact papers – published by researchers from the Radboudumc – will be discussed.

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Mitral annular disjunction as a common result of cardiac imaging

With the technological advances of the last decades, detailed cardiac imaging has become available. Scientists from the Radboud University Medical Centre and the United Kingdom have analysed the presence of mitral annular disjunction on cardiac magnetic imaging (CMR) in participants of the UK Biobank project [1]. Their research was published in JACC Cardiovascular Imaging (Impact factor 16.55). In the UK Biobank project, over 500.000 individuals between 40 and 69 years old in the United Kingdom underwent extensive testing, including genome-wide genotype data. Data from this project was used in this research, which assessed the prevalence of mitral annular disjunction in a study population (predominantly) without a history of cardiac disease. 2,607 participants, who received CMR during the UK Biobank project, were included. The average age of the participants was 61 years. Out of the 2,607 participants, 68 had cardiac arrhythmias, of which six were ventricular arrhythmias. Four participants had survived a cardiac arrest. Other participants had no known risk factors for cardiac disease. In 76% of the participants, a disjunction of the mitral annulus was seen. However, the incidence differed depending upon the location of the disjunction. Inferolateral disjunction was seen in only 5% of the participants. However, disjunction in other locations was found commonly - in 72% of the participants - which raises the question of whether these disjunctions are as pathognomonic as previously thought. The high prevalence of mitral annular disjunction suggests that it is a relatively harmless finding in this age cohort.

Tetraspanin CD37 as a key mediator of fatty acid metabolism in aggressive B-cell lymphoma

CD37-deficiency is associated with a poorer prognosis in diffuse large B-cell lymphoma (DLBCL). This is hypothesised to be due to an alteration in the cell's metabolism, where CD37-deficient DLBCL relies on fatty acid (FA) metabolism, as opposed to glycolysis. Peeters et al. studied the role of CD37 in FA metabolism in DLBCL, which was published in Nature Communications (impact factor 17.7) [2]. Their research suggests that CD37-deficient tumours are indeed dependent upon FA metabolisation, which is mediated through the fatty acid transporter protein 1 (FATP1). This could provide a survival advantage for malignant cells. The switch in metabolism provides energy even under hypoxic conditions, which is often seen in tumours. The switch to FA metabolism was shown using cell lines and animal models. CD37 knock-out (KO) cells showed increased uptake of the fatty acid palmitate, in comparison to DLBCL-positive cells. Furthermore, the CD37 KO cells exhibited an increased mitochondrial respiratory capacity after the administration of palmitate. This effect is thought to occur through an interaction between FATP1 and CD37. FATP1 was prominently expressed in DLBCL cells and colocalized with CD37. Furthermore, it was shown that DLBCL CD37-KO cell lines show a dose-dependent increase in lipid droplets after the administration of palmitate. This seems to suggest that these CD37-deficient cells can form an energy reserve. The FAs, stored in these lipid droplets, could namely be metabolized under hypoxic, nutrient-deficient circumstances, resulting in an additional survival advantage. Therefore, FA metabolism could be a therapeutic target. This was also tested in this study, using a carnitine-palmitoyl-transferase inhibitor. Carnitine-palmitoyl-transferase transports fatty acids into the mitochondria. A dose-dependent decrease in viability and proliferation of CD37KO cells was seen in vitro after the administration of the inhibitor. Thus, this study provides a molecular framework of the intracellular functions of CD37, which could lead to promising therapeutic consequences in the future.

Increased risk of kidney injury for children with a solitary functioning kidney

A solitary functioning kidney (SFK) can be congenital (cSFK) or acquired (aSFK). In both cases, children with SFK are at risk of long-term kidney injury. However, the risk factors are not yet clear. Therefore, Groen in 't Woud et al. conducted the Solitary Functioning Kidney: Aetiology and Prognosis (SOFIA) study [3]. Their study, published in Kidney International (impact factor 19), included 944 children with SFK, diagnosed between 1993 and 2020. The average duration of follow-ups was 12.8 years. The outcome was the incidence of kidney injury, indicated by the urine protein/creatinine ratio, estimated glomerular filtration rate, blood pressure, and the use of antihypertensive or proteinuric medication. At the age of eighteen, 75% of patients with cSFK and 80% of patients with aSFK had at least one indicator of kidney injury. Up to 39% and 37% of the patients with cSFK and aSFK, respectively, developed severe kidney failure. Risk factors for the development of kidney injury were female sex (HR for cSFK/aSFK 1.3, 95% CI 1.1-1.7), severe congenital abnormalities of the kidney and urinary tract (HR 1.3/1.3, 95% CI 1.0-1.7), and high BMI at last follow-up (HR 1.8/1.6, 95% CI 1.0-2.6). Risk factors for severe kidney injury included severe congenital abnormalities of the kidney and urinary tract (HR cSFK/aSFK 1.6/1.5, 95% CI 1.0-2.3), SFK length below p50 (HR 2.0/2.0 95% CI 0.5-8.0), and a high BMI (HR 2.9/2.4, 95% CI 1.2-4.8). Patients with hypodysplasia, i.e. a small or underdeveloped kidney, had a lower risk of severe kidney injury (HR cSFK/aSFK 0.7/0,5, 95% CI 0.3-1.0), as did patients with fetal multicystic dysplastic kidney (HR 0.7/0.7 95% CI 0.4-0.9). This study suggests that children with SFK should receive long-term follow-up, with an emphasis on lifestyle management.

References

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