

### Degenerative alterations in RVOT samples – what to learn from histopathological analysis?

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**Objectives:** Many children with reconstructive surgery of the RVOT during childhood need re-operation mostly due to re-obstruction. Focusing on histological correlation of degenerative alterations, we examined the calcification degree, number of nuclei per mm<sup>2</sup> as well as the expression of tissue inhibitors of metalloproteinases (TIMPs) and matrix metalloproteinases (MMPs) in explanted RVOT samples. □

**Methods:** RVOT samples from 38 patients (male: n=24, 63%; female: n=14, 37%), who underwent re-operation of the RVOT at a median age of 16 years [2-60 years] (median 14.2 years [1.8-49 years] after primary surgery), were gathered. After standardized specimen preparation, staining was performed with alizarin-red dye to visualise calcification. Nuclei were identified using nuclear fast red staining. Additionally, immunohistochemistry was performed focusing on TIMP1 and MMP9. Calcification intensity was quantified in a standardized fashion. Furthermore, present nuclei per mm<sup>2</sup> as well as TIMP and MMP expression were analysed microscopically. □□



**Results:** Indications for primary surgery were Tetralogy of Fallot (n=21; 55.3%), double outlet right ventricle (n=3; 7.8%), truncus arteriosus communis (n=2; 5.3%) and other malformations of the RVOT and pulmonary arteries (n=11; 28.9%). During re-operation either allografts (n=3), autologous (n=6) and bovine (n=16) tissue or synthetic material (n=5) that was previously used for a transannular patch repair (n=22) and reconstruction of the RVOT (n=16) was explanted. 18 specimens (52.6%) showed severe calcifications macroscopically.

Bovine explants showed a higher degree of calcification than autologous tissue (p=0.004) but were less calcified than synthetic materials such as GORETEX® or DACRON® (p=0.001). Amount of nuclei per mm<sup>2</sup> did not differ significantly between the 3 groups (human: 11.31/mm<sup>2</sup>; bovine: 10.20/mm<sup>2</sup>; synthetic: 10.25/mm<sup>2</sup>). TIMP1 and MMP9 showed positive results in all samples. □□

**Conclusions:** Bovine samples seem to be more susceptible to calcification than autologous tissue. If transannular patch repair is needed, we recommend to use autologous tissue at primary repair. Nuclei per mm<sup>2</sup> were equal in all groups. The presence of MMP9 indicates processes of angiogenesis and neovascularisation, while TIMP1 expression is important for the integrity of connective tissue. To further classify degenerative alterations, complementary examination will be performed. □