

Trans-Radial Coronary Interventions: A “Win-Win” for Both Patient and Operator

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Trans-radial access for coronary catheterization and intervention has gained much popularity in recent years both in Israel and worldwide [1], mainly because of fewer vascular complications and better patient comfort. In the current issue of *IMAJ*, Goldberg et al. [2] describe a rare complication of the trans-radial approach for cardiac catheterization.

Campeau in 1989 [3] and later Klemeneij and Laarman in 1993 [4] successfully attempted diagnostic cardiac catheterization and percutaneous coronary intervention, respectively, using the radial artery. Since these seminal reports, the use of trans-radial intervention has gradually gained acceptance. Support for this practice has stemmed from numerous small trials and observational studies that demonstrated several advantages of trans-radial over trans-femoral intervention, such as early ambulation, shorter hospital stay, fewer access-site vascular complications, and less major hemorrhage and need for transfusions [5]. Furthermore, in a meta-analysis of ten randomized trials Joyal and co-authors [6] demonstrated reduced short term-mortality in patients undergoing primary PCI using the trans-radial approach. However, and very disappointingly, a large randomized trial of 7021 patients presenting with acute

coronary syndrome and undergoing PCI did not show any significant benefit of the trans-radial approach on major bleeding, MACE or mortality [7].

Recently, a randomized study comparing trans-radial to trans-femoral intervention in patients undergoing primary PCI for acute ST-elevation myocardial infarction was presented (TCT 2012). No differences were noted between the radial and femoral approaches in rates of death, repeated myocardial infarction, and stroke; however, a significant 80% relative risk reduction was observed in the rate of bleeding.

Bleeding, especially major, has been described in several trials and in a variety of clinical settings as an independent predictor of short and long-term outcome [8]. In the context of PCI, early bleeding may result in the interruption of dual antiplatelet therapy leading to thrombotic coronary events. Furthermore, bleeding itself may also be prothrombotic [9].

Much variability in the use of trans-radial intervention remains between countries and between centers and operators. While it is the preferred route for cardiac catheterization and PCI in some European countries today, in the United States fewer than 10% of procedures are performed using the radial route. Over the last decade the use of trans-radial intervention in Israel has grown in popularity to the extent that about one-third of all coronary procedures in patients with acute coronary syndromes are performed using the radial approach [1].

Technically, the radial approach can be challenging and requires a learning curve.

PCI = percutaneous coronary intervention
MACE = major adverse cardiac event

The main obstacle for this access is radial spasm, which in the majority of cases can be overcome by proper technique and the use of arterial vasodilators. Second, cannulation of coronary ostia can also be challenging due to anatomical variation of the great arteries of the aorta and lack of dedicated catheters. However, once mastery of the radial approach is obtained, it is difficult to conceive of a return to indiscriminate use of the femoral approach. Vascular complications are reported much less frequently with the use of the radial approach. Nonetheless, this report by Goldberg et al. [2] reminds us that no technique is infallible and that complications, while infrequent, do occur.

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Capsule

Phosphorylation of FOXP3 controls regulatory T cell function and is inhibited by TNF α in rheumatoid arthritis

Regulatory T (Treg) cells suppress autoimmune disease, and impaired Treg cell function is associated with rheumatoid arthritis. Nie and team demonstrate that forkhead box P3 (FOXP3) transcriptional activity and, consequently, Treg cell suppressive function are regulated by phosphorylation at Ser418 in the C-terminal DNA-binding domain. In rheumatoid arthritis-derived Treg cells, the Ser418 site was specifically dephosphorylated by protein phosphatase 1 (PP1), whose expression and enzymatic activity were induced in the inflamed synovium by tumor necrosis factor- α (TNF α), leading to impaired Treg cell function. Moreover, TNF α -induced Treg cell dysfunction

correlated with increased numbers of interleukin-17 (IL17)+ and interferon- γ (IFN γ)+CD4+ T cells within the inflamed synovium in rheumatoid arthritis. Treatment with a TNF α -specific antibody restored Treg cell function in subjects with rheumatoid arthritis, which was associated with decreased PP1 expression and increased FOXP3 phosphorylation in Treg cells. Thus, TNF α controls the balance between Treg cells and pathogenic TH17 and TH1 cells in the synovium of individuals with rheumatoid arthritis through FOXP3 dephosphorylation.

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Eitan Israeli

Capsule

Aggregates as a mechanistic insight into the pathogenesis of FTL/ALS

Several recent papers have revealed the unexpected genetic and pathological overlap between frontotemporal lobar degeneration (FTLD) and amyotrophic lateral sclerosis (ALS). The most common genetic cause is the GGGGCC hexanucleotide repeat expansion upstream of the *C9orf72* coding region affecting about 10% of all patients. It is currently unknown how repeat expansion might lead to neurodegeneration. *C9orf72* patients show two distinct types of ubiquitinated inclusions in the central nervous system, one of which was identified as phosphorylated TDP-43 protein. However, all inclusions in the cerebellum and most inclusions

in the hippocampus and neocortex lack TDP-43, and the actual disease protein is unknown. Mori et al. discovered that most of these characteristic inclusions contain poly-(Gly-Ala) and, to a lesser extent, poly-(Gly-Pro) and poly-(Gly-Arg) dipeptide-repeat proteins that are generated by non-ATG-initiated translation from the expanded GGGGCC repeats in three reading frames. The findings yield mechanistic insight into the pathogenesis of FTL/ALS with *C9orf72* repeat expansions and directly link this common mutation to the characteristic pathology.

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Eitan Israeli

Capsule

Lowered serum amyloid- β 1-42 autoantibodies in individuals with lifetime depression

Reduced levels of naturally occurring autoantibodies against amyloid- β (A β) have been described in Alzheimer's disease (AD). Lifetime depression doubles the risk of AD, thus these autoantibodies may also be reduced in this group. Maetzler and colleagues measured serum immunoglobulin G autoantibody titers against A β 1-42, S100b and α -synuclein in 214 individuals with depression and 419 controls. Titers against A β 1-42 were lower

in individuals with lifetime depression (5544.6 ± 389.3) compared to controls (7208.7 ± 482.4 , $P = 0.048$). Titers against S100b and α -synuclein were comparable between the cohorts. These data suggest an AD-like impairment of the humoral immune response in a relevant proportion of individuals with depression.

J Alzheimers Dis 2012; 32 (1): 95

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