

## Angiographic Functional Characterization of the Coronary Sinus

Ricardo Krakover MD, Alexander Blatt MD, Alberto Hendler MD, Itzchak Zisman MD, Meir Reicher MD, Josef Gurevich MD, Eliahu Peleg MD, Zvi Vered MD and Edo Kaluski MD

Interventional Cardiology Unit, Department of Cardiology, Assaf Harofeh Medical Center, Zerifin, Israel  
Affiliated to Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

**Key words:** coronary sinus, coronary venous drain

### Abstract

**Background:** Coronary sinus is a venous conduit with dynamic and unclear function with regard to coronary circulation.

**Objectives:** To describe the dynamic changes of the coronary sinus during the cardiac cycle.

**Methods:** The angiographic feature of the coronary sinus was evaluated in 30 patients undergoing diagnostic and therapeutic coronary angiography.

**Results:** Prolonged angiographic imaging following coronary injections permitted accurate demonstration of the coronary sinus in all 30 patients. We report, for the first time, that the coronary sinus can be divided into two angiographic functional/anatomic portions, upper and lower. The lower part is prone to a highly dynamic contraction/relaxation pattern, observed in 12 of the 30 patients, while 10 patients had normal and 8 had low contractile pattern on angiography. Clinical assessment of these patients did not identify an association with this motion pattern.

**Conclusions:** The coronary sinus is an important anatomic/functional structure that should be further investigated in patients with various forms of heart disease.

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The coronary sinus is a venous conduit, which drains between 80% and 85% of unsaturated blood of the left ventricle. Its main clinical use is during therapeutic and diagnostic electrophysiology procedures and for reverse cardioplegia during cardiac surgery [1]. The coronary sinus length ranges from 2.5 to 6 cm and is located in the posterior wall of the heart. The lumen is progressively dilated to a maximal inner diameter reaching the right atrium. Close to its distal portion there is a semilunar structure, the Tebesius valve, which does not completely occlude the sinus; however, it is occasionally atrophic.

The sinus endothelium is similar to that of the right atrium, but its wall has a specific anatomy [2]. During angiography the coronary sinus is better visualized in the right anterior oblique and left anterior oblique projections with cranial or caudal angulation. Its tract is fully visualized following a few cardiac cycles after injection of contrast material. At these views the coronary sinus is divided into two parts: above and below the left posterior vein. The upper portion appears to be more static, however the lower portion is most active, showing marked changes during the cardiac cycle.

Reports on coronary sinus functional anatomy are scarce. The only descriptions are of anomalies with little significance in adult coronary circulation (especially in the presence of atherosclerosis of epicardial arteries). In this article we describe the dynamic changes of the coronary sinus during the cardiac cycle.

### Patients and Methods

We analyzed the angiographic venous phase in 30 consecutive patients undergoing coronary angiography for diagnosis and treatment of coronary artery disease. Patients after cardiac surgery were excluded. The patients were treated with aspirin, platelet inhibitors, nitrates, and beta or calcium channel blockers, which were not discontinued prior to cardiac catheterization. Eight patients had stable angina and 22 had acute coronary syndromes including myocardial infarction. The average age of the group was  $61.7 \pm 10.1$  years; ejection fraction was  $47.7 \pm 4.8\%$ . Ten patients had single-vessel disease, 6 had double-vessel disease and 9 had triple-vessel disease; 3 patients had normal coronary arteries and 2 had left main disease. Hypertension, dyslipidemia and diabetes were present in 75%, 80% and 29% respectively, while 45% of the patients had all three risk factors.

### Technique of angiographic evaluation

During routine coronary angiography the coronary sinus was evaluated in at least two views – cranial RAO or cranial LAO. On both views the tract and affluents are well visualized with the drainage into the right atrium after six to eight cycles on average. The left posterior vein divides the sinus into two portions: upper and lower. According to the dynamic variations observed in the lower part we divided the patients into three groups.

- Passive coronary sinus (P) with minimal or no changes during the cardiac cycle [Figure 1].
- Normal-response coronary sinus (N) with rhythmic changes during the cardiac cycles [Figure 2]. (Between 20% and 40% dynamic stenosis by angiographic evaluation).
- Hyperactive coronary sinus (H) with marked cyclic changes in which the lumen is almost completely obliterated [Figure 3]. (More than 60% dynamic stenosis by angiographic evaluation).

### Results

The coronary sinus could be accurately imaged in all 30 patients. Careful angiographic evaluation permitted separation of the coronary sinus into two parts: upper and lower. We observed that the upper part of the sinus was relatively unchanged throughout the cardiac cycle. The lower part, however, was highly variable: in 12 patients a hyper-

RAO = right anterior oblique

LAO = left anterior oblique

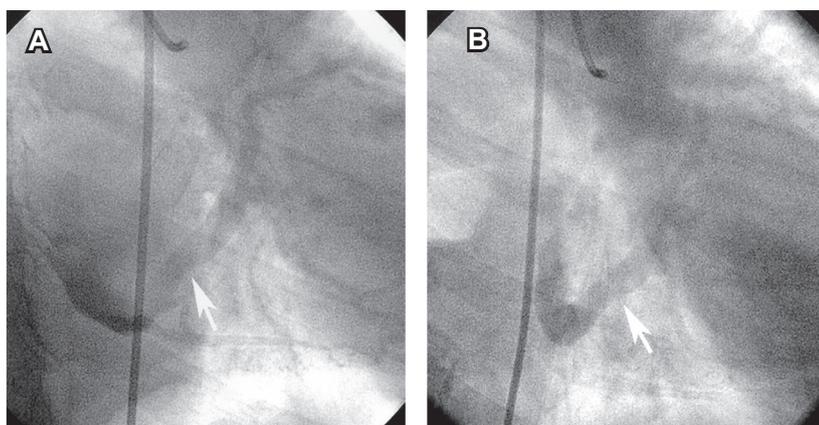


Figure 1. Passive coronary sinus

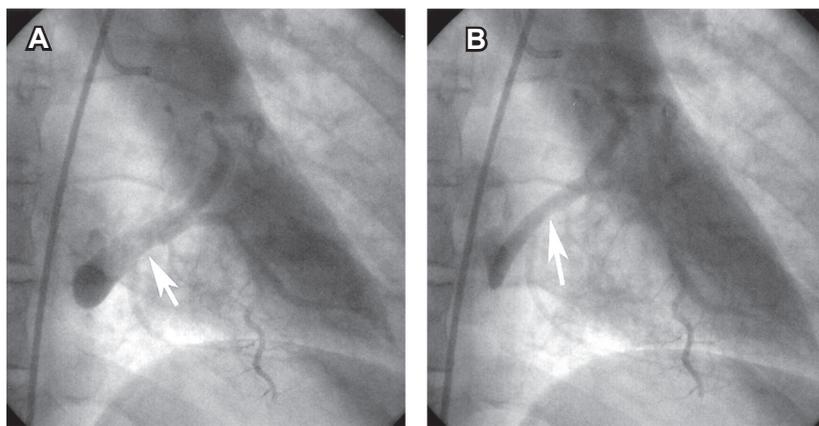


Figure 2. Normal response coronary sinus

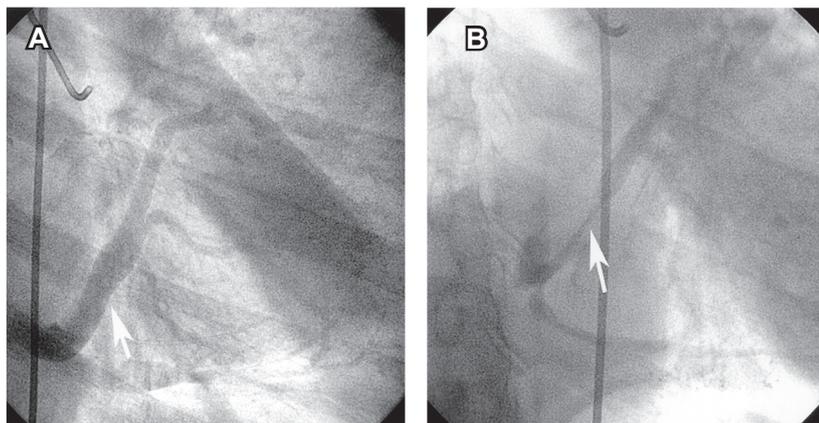


Figure 3. Hyperactive coronary sinus

Table 1. Clinical and angiographic findings

	Coronary sinus		
	Hyperdynamic	Normal	Passive
<b>Clinical presentation</b>			
Asymptomatic	1		
Unstable angina	5	6	2
Stable angina	3	2	3
Acute myocardial infarction	4	1	3
<b>No. of vessels</b>			
Normal coronary arteries		2	1
Left main stenosis		1	1
1 vessel disease	4	2	4
2 vessel disease	2	2	2
3 vessel disease	5	3	1

dynamic contraction/relaxation pattern was observed in the lower part, as compared to 10 patients in whom "normal" changes occurred and 8 patients in whom a significantly reduced contraction was noted.

An attempt to correlate this observation with various clinical parameters did not yield any significant findings. Table 1 presents the clinical and angiographic findings of these patients.

## Discussion

The main purpose of the current communication is to describe, for the first time, the dynamic motion of the coronary sinus. The coronary sinus has been extensively investigated in studies dealing with obtaining blood samples of coronary venous blood, such as lactate [3]. It is also an important location during electrophysiologic studies [4]. Temporary pacemaker electrodes also tend to enter the coronary sinus, although this can easily be overcome with fluoroscopy guidance.

More recently, the cardiac venous system has gained attention with the introduction of bi-ventricular pacing systems [5]. During routine cardiac catheterization the venous system is rarely investigated. Recently, the Thrombolysis In Myocardial Infarction group recommended that physicians evaluate the degree of "coronary blush." This measure of myocardial perfusion by semi-quantitative assessment includes tissue and opacification after dye injection of epicardial coronary arteries [6].

Barcelo et al. [2] pointed out that the coronary sinus is not a simple vein. Our finding confirms that observation by showing the dynamic variation of the coronary sinus lumen, probably as part of a physiologic phase: the draining and conducting of blood. An exaggerated response to this mechanism could potentially modify cyclic coronary circulation and perfusion, causing slow flow phenomena or other pathophysiologic changes in patients with normal coronary arteries or with other pathology, such as abnormal relaxation of the ventricular wall. Moreover, these changes may uncover "dormant conduction fibers," which have been implicated with the etiology of arrhythmias.

We recently started to routinely investigate the flow in the coronary venous system during coronary angiography procedures. The main limitation of the current report is that the evaluation was not quantitative. The Quantitative Coronary Angiography method was shown to be inaccurate because of the large difference between the reference catheter and the coronary sinus.

Further investigation is needed to correlate these angiographic findings with clinical syndromes. In spite of these limitations we believe that this observation is the first angiographic dynamic description of coronary sinus. These dynamics are striking and should be further investigated.

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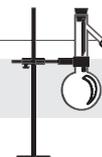
**Correspondence:** Dr. R. Krakover, Interventional Cardiology Unit, Dept. of Cardiology, Assaf Harofeh Medical Center, Zerifin 70300, Israel.

Phone: (972-8) 977-9735

Fax: (972-8) 977-9738

email: rkrakover@asaf.health.gov.il

## Research Projects



### **<sup>18</sup>Fluorine-labeled anti-androgens for in vivo imaging in prostate cancer using positron-emission tomography (PET)**

M. Guzin PhD<sup>1</sup>, E. Mishani PhD<sup>2</sup>, I. Leibovitz MD<sup>3,6</sup>, M. Gutman MD<sup>4,6</sup> and E. Even-Sapir MD PhD<sup>5,6</sup>

<sup>1</sup>Faculty of Chemistry, Tel Aviv University, Ramat Aviv, Israel

<sup>2</sup>Cyclotron Unit, Hadassah University Hospital, Jerusalem, Israel

Departments of <sup>3</sup>Urology and <sup>4</sup>Surgery A, Sapir Medical Center, Kfar Saba, Israel

<sup>5</sup>Department of Nuclear Medicine, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

<sup>6</sup>Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

**Background:** Most prostate cancers express androgen receptors (AR) and by targeting that receptor with PET imaging, prostate cancer and its metastases can be seen. However, the current PET tracer, F18-FDG, commonly used in tumor imaging, is not appropriate for detecting prostate cancer which is often non-FDG avid. Considering the importance of properly diagnosing and treating prostate cancer, development of a new PET AR ligand is warranted. An AR-based PET tracer may potentially enable differentiation between patients responsive to anti-androgen therapy (AR-PET positive) and non-responders; and differentiation between candidates for surgical removal of the tumor and the prostate (no evidence of metastatic disease by AR-PET) and non-candidates.

**Objectives:** To develop PET radio pharmaceuticals for *in vivo* determination of androgen receptor expression in patients with prostate cancer.

**Methods:** Fluorine-containing analogs of non-steroidal AR antagonists approved

for use in humans were synthesized and tested *in vitro* for their binding affinity to AR. Lead compounds with high AR affinity were radiolabeled with <sup>18</sup>F and tested *in vitro* for binding to AR and for stability.

**Results:** In attempts to prepare <sup>18</sup>F-labeled anti-androgen compounds for prostate cancer PET imaging, R-enantiomer [<sup>18</sup>F]-fluoro-hydroxyflutamide was selected as a first synthetic target. The synthesis was based on the chirality-inducing auxiliary approach, where D-proline was selected as such an auxiliary. This compound was synthesized in multigram quantities in several batches with yields that were appreciable and comparable to previous reports. Most of the intermediates were obtained at a purity higher than that reported in the literature, based on melting point comparison. <sup>1</sup>H and <sup>13</sup>C NMRs as well as MS, FTIR and optical rotation were routinely measured for all intermediates. Seven different compounds were tested as targets for fluorination. Interesting results were obtained from at-

tempts to utilize silver fluoride. The results obtained suggest that after bromide removal by the silver ion, a formed carbocation can be attacked intramolecularly by anilide nitrogen to form a four-membered ring cyclic product, or the oxygen at the alpha position can also close an epoxide ring. These side products were identified by MS and NMR. Similarly, attempts to replace the bromide with a good leaving group in order to perform nucleophilic fluorination were unsuccessful for the same reasons. Therefore, another approach for labeling these potent compounds was adapted and the labeling was successfully performed on the aromatic ring via a three-step radiosynthesis. The first labeled androgen biomarker was obtained and purified and identified by high performance liquid chromatography.

**Conclusions:** The compounds synthesized have the potential for being new potent anti-androgen agents and we plan to evaluate their biological activity in the near future.

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