Origin of great cardiac vein and coronary sinus drainage within the left ventricle

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ROBERTS, DOUGLAS L., HIROE K. NAKAZAWA, AND FRANCIS J. KLOCKE. Origin of great cardiac vein and coronary sinus drainage within the left ventricle. Am. J. Physiol. 230(2): 486-492. 1976.—The relative contributions of left anterior descending (LAD) and left circumflex (LC) arterial inflow to blood sampled at various points within the great cardiac vein (GCV) and coronary sinus (CS) have been investigated in open-chest dogs. Dissolved helium (He) and hydrogen (H2) were infused into external circuits perfusing the LAD and LC, respectively, and their steady state concentrations were measured chromatographically at various points within the GCV and CS. Under basal conditions GCV H2 averaged only 5% of mid-CS H2 and did not change greatly during alterations of preload and afterload or during selective LAD or LC obstruction and vasodilation. The relationship of mid-CS He to GCV He was more variable under basal conditions and changed noticeably during selective changes in LAD or LC inflow. Appreciable amounts of He were present consistently in left marginal vein drainage. We conclude that: 1) GCV blood is remarkably free of LC inflow in both normal and abnormal physiological states; 2) the origin of mid-CS blood is more variable, both from animal to animal and in individual animals before and after interventions; 3) a portion of LAD drainage normally reaches the CS through circumflex venous branches rather than the GCV.

coronary venous drainage; anterior descending vs. circumflex outflow; regional venous sampling; coronary venous interconnections


METHODS

THE EXPERIMENTAL PREPARATION IS SHOWN IN FIG. 1. MONGREL DOGS WEIGHING FROM 20 TO 53 KG WERE ANESTHETIZED WITH PENTOBARBITAL SODIUM, INTUBATED, AND PLACED ON A CONSTANT-VOLUME RESPIRATOR. THE HEART WAS EXPOSED THROUGH A LEFT THORACOTOMY AND SUSPENDED IN A PERICARDAK CRADLE. THE INITIAL 1–1.5 CM OF THE ANTERIOR DESCENDING AND CIRCUMFLEX DIVISIONS OF THE LEFT CORONARY ARTERY WERE ISOLATED AND PREPARED FOR PERFUSION THROUGH EXTERNAL CIRCUITS. THE LATTER WERE DESIGNED TO ALLOW SELECTIVE INFUSION OF DIFFERENT SOLUBLE INERT GAS TRACERS INTO THE TWO ARTERIAL BEDS. BOTH CIRCUITS WERE SUPPLIED WITH BLOOD AT THE ANIMAL'S OWN AORTIC PRESSURE THROUGH A Y-SHAPED CANNULA INSERTED INTO THE LEFT SUBCLAVIAN ARTERY. EACH INCLUDED AN INFUSION PORT AND MIXING CHAMBER AND TERMINATED IN A 2-MM-ID METAL CANNULA. THE CANNULAS WERE SECURED IN THE ANTERIOR DESCENDING AND CIRCUMFLEX ARTERIES AFTER LIGATION OF THE PROXIMAL ARTERIAL SEGMENTS. IN SEVERAL CASES AN EXTRACORPOREAL SINE-WAVE ELECTROMAGNETIC FLOWMETER (MODEL 2031-T, BIOTRONEX LAB. INC.) WAS INCLUDED IN ONE OR THE OTHER OF THE PERFUSION CIRCUITS UPSTREAM TO THE INFUSION PORT AND MIXING CHAMBER. PRELIMINARY IN VITRO TESTS INDICATED THAT THE PRESSURE DROP ACROSS EACH CIRCUIT WAS ONLY 5 MM Hg AT A FLOW OF 50 ML/MIN AND THAT CONCENTRATIONS OF INFUSED TRACERS WERE CONSTANT WITHIN ±5–10% DISTAL TO THE MIXING CHAMBERS.

IN SIX ANIMALS, VENOUS BLOOD WAS SAMPLED THROUGH AN 8F SHIREY CATHETER (MODEL 5436, U.S. CATHETER & INSTRUMENT CO., BILLERICA, MASS.) AT THE ORIGIN OF THE GREAT CARDIAC VEIN AND, AS THE CATHETER WAS WITHDRAWN IN STEPSWISE FASHION, AT THREE OR FOUR ADDITIONAL POINTS WITHIN THE CORONARY SINUS.

IN 23 ANIMALS, TWO SHIREY CATHETERS WERE EMPLOYED SIMULTANEOUSLY, ONE BEING POSITIONED WITHIN 0.5–1.0 CM OF THE ORIGIN OF THE GREAT CARDIAC VEIN AND THE OTHER 2–3 CM WITHIN THE CORONARY SINUS. THE LOCATIONS OF THESE...
FIG. 1. Experimental preparation for studying origin of great cardiac vein and coronary sinus drainage. Tips of 2 catheters inserted into coronary sinus lie near origin of great cardiac vein and in midcoronary sinus, respectively. Dashed lines illustrate potential venous interconnections between areas of myocardium perfused by anterior descending and circumflex divisions of left coronary artery. MC, infusion port and mixing chamber; LCA, left coronary artery; LAD, anterior descending division of left coronary artery; LC, circumflex division of left coronary artery; DIAG, proximal diagonal branch of LAD (or of main LCA itself); GCV, great cardiac vein; CS, coronary sinus, AIV, anterior interventricular vein; LMV, left marginal vein; PIV, posterior interventricular vein.

catheters are subsequently referred to as the GCV and mid-CS positions. The GCV position was chosen to represent the most selective sample of left anterior descending drainage ordinarily available in closed-chest animals and man. The CS position was intended to provide as complete as possible a sample of total left ventricular outflow while still avoiding right atrial admixture (15). As expected, on postmortem examination, the CS position never appeared to include drainage from the posterior interventricular veins.

In four animals, a Shirey catheter was positioned at the origin of the GCV and a second, smaller polyethylene catheter (1.25 mm OD) was manipulated into the left marginal vein and positioned so that its distal tip was 2–3 cm upstream of the junction of the marginal vein with the CS. Observations were made before and after ligation of visible epicardial vascular connections between the anterior descending and circumflex beds. Catheter positions were checked frequently in all experiments and did not change spontaneously.

Solutions containing dissolved inert gas tracers were prepared by bubbling helium (He) and hydrogen (H\textsubscript{2}) through individual flasks containing isotonic saline for 20 min. The He and H\textsubscript{2} solutions were transferred into glass syringes for delivery by gear-driven infusion pumps into the anterior descending and circumflex perfusion circuits, respectively. For each determination of venous drainage pattern, 2.0-ml venous samples were drawn in triplicate 15 min after the onset of simultaneous infusion of both tracers at a rate of 3.6 ml/min. Peak rates of venous withdrawal were less than 10 ml/min. Concentrations of He and H\textsubscript{2} in each venous sample were quantitated by gas chromatography and results expressed as the ratios between GCV and CS H\textsubscript{2} concentrations and CS and GCV He concentrations. As discussed subsequently, the GCV-to-CS H\textsubscript{2} ratio reflects the degree to which left circumflex outflow enters the great cardiac vein and the CS-to-GCV He ratio reflects the degree to which anterior descending outflow is diluted by circumflex outflow in the coronary sinus. The chromatographic technique was identical to that previously described for H\textsubscript{2} analysis (23) except that a 12-foot rather than a 6-foot column of activated charcoal was employed (the longer column being needed to achieve adequate separation of H\textsubscript{2} from He).

After the above experiments, three additional animals were studied with thermal indicator and in situ temperature measurement in order to verify findings relating to venous interconnections between myocardium supplied by the anterior descending and circumflex arteries. The same external perfusion circuits were employed but the venous sampling catheters were replaced with two 0.97-mm-OD thermistor catheters having a response time of 0.1 s (model 520X, Yellow Springs Instrument Co., Yellow Springs, Ohio). Thermistor resistances were measured with Wheatstone bridges; precalibration of the two catheters indicated that temperature-related changes in resistance were within a few percent of each other between 35 and 39°C. The thermistor catheters were positioned in the anterior interventricular vein near the atrioventricular groove and in the left marginal vein 2–3 cm upstream of its junction with the CS. Recordings were made during injection of room-temperature saline into the anterior descending arterial perfusion circuit, the circumflex arterial perfusion circuit, and the great cardiac vein (through another conventional catheter).

RESULTS

Figure 2 illustrates relative concentrations of He and H\textsubscript{2} at various points within the coronary venous system in the six animals in which blood was sampled at several positions sequentially with a single catheter. The highest concentration of each tracer has arbitrarily been assigned a value of 100 and other concentrations scaled accordingly. Hydrogen concentrations are only a few percent of maximum levels in the great cardiac vein but increase progressively as outflow is sampled nearer the CS ostium. Helium concentrations are highest in the GCV and decrease as blood is sampled nearer the CS ostium.

Table 1 lists findings in the four animals in which blood was sampled simultaneously in the great cardiac vein and the left marginal vein. The H\textsubscript{2} concentrations in the great cardiac vein are only 2–5% of H\textsubscript{2} concentrations in the marginal vein, whereas He concentrations in the marginal vein are 16–45% of those in the GCV. After ligation of visible vascular interconnections between the anterior descending and circumflex beds, He concentrations in the marginal vein fall to 2–5% of those in the GCV.
FIG. 2. Relative concentrations of H₂ and He at various points within coronary venous system. Values for H₂ are listed first, followed by corresponding values of He in parentheses. In each case, great cardiac vein-coronary sinus system was traced from its image on a fluoroscopic monitor with animal in a 45° LAO position. Tracing was facilitated by small injections of contrast material (meglumine diatrizoate). Arrows indicate positions of tip of sampling catheter for individual He and H₂ measurements.

TABLE 1. Relative concentrations of helium and hydrogen in great cardiac and left marginal veins

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>H₂ GCV/H₂ LMV</th>
<th>He GCV/He LMV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.02</td>
<td>0.16</td>
</tr>
<tr>
<td>2</td>
<td>0.02</td>
<td>0.17</td>
</tr>
<tr>
<td>3</td>
<td>0.02</td>
<td>0.25</td>
</tr>
<tr>
<td>4</td>
<td>0.06</td>
<td>0.45</td>
</tr>
<tr>
<td>After ligation of epicardial vascular interconnections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td>4</td>
<td>0.05</td>
<td>0.06</td>
</tr>
</tbody>
</table>

H₂ GCV/He GCV = ratio of helium concentration in left marginal vein to that in great cardiac vein; H₂ LMV/He LMV = ratio of hydrogen concentration in great cardiac vein to that in left marginal vein.

Figure 3 illustrates a representative tracing from an animal in which room-temperature saline was employed as indicator and intravascular temperatures were measured directly in the anterior interventricular and left marginal veins. Noticeable cooling occurs in the left marginal vein after saline injection into the circumflex perfusion circuit, but anterior interventricular temperature is unchanged. After injection of saline into the anterior descending perfusion circuit, both venous temperatures decrease. Identical findings were obtained in each of the three animals studied. As also illustrated in Fig. 3, marginal vein temperature never decreased detectably after GCV injection of saline.

Figure 4 illustrates findings under basal conditions in the 23 animals in which He and H₂ concentrations were measured simultaneously near the origin of the GCV and in the mid-CS. The GCV H₂ concentration was less than 6% of mid-CS H₂ concentration in 17 of 23 animals and averaged only 5.3 ± 5.1 (SD)% of mid-CS H₂ concentration for the entire group. The CS He concentrations were uniformly lower than GCV He concentrations, but showed considerable variation, averaging 53 ± 12% of GCV levels. Spontaneous variations in relative concentrations of tracers over 90-min periods are shown in Fig. 5. None of the three animals studied showed an appreciable change in the ratio of GCV to CS H₂ concentration. Ratios of CS to GCV He did vary, by absolute levels of 0.19, 0.07, and 0.12.

Figure 6 illustrates relationships between GCV and mid-CS tracer concentrations before and after changes in afterload and preload. Increments in afterload were produced by constriction of the descending aorta sufficient to increase proximal systolic pressure by 57 ± 16% (85 ± 14 mmHg to 132 ± 15 mmHg). Preload changes were effected by saline infusions sufficient to increase mean left atrial pressure from 5.2 ± 2.7 to 20 ± 1.6 mmHg. Changes in the ratio of CS He concentration to GCV He concentration were variable after both interventions and did not achieve statistical significance (paired t). The GCV-to-CS H₂ ratios either showed no
ORIGIN OF GCV AND CS DRAINAGE WITHIN LEFT VENTRICLE

0.80 - 0.60 - 0.40 - 0.20 - 0.00 -

HeGCV

H2 GCV

H2CS

~~r.-~.r;:? ----*---- _

0.00 -

30 60 90

TIME (MIN)

FIG. 5. Spontaneous variations in ratios of tracer concentrations under basal conditions. Solid, dotted, and dashed lines illustrate corresponding data for He and H2 in each of 3 animals studied.

0.085 µg/kg per min. Recirculation of vasodilator was negligible because of dilution in the remainder of right heart output and normal clearance of prostaglandin E1 within the pulmonary circulation (10, 18, 22). The LAD inflow increased by 75, 89, and 84% in three animals; the ratio of GCV to CS H2 concentration did not change noticeably but CS He increased from 56 ± 6% to 68 ± 5% of GCV He (0.05 < P < 0.10). Flow increments were measured in three of four animals during circumflex infusion and were 91, 100, and 67% of control values. Ratios of GCV to CS H2 concentration did not change significantly but CS He concentration decreased from 64 ± 5.4% to 48 ± 7.8% of GCV He concentration (P < 0.01).

DISCUSSION

Most previous studies of coronary venous drainage patterns have compared outflow from the coronary sinus and outflow from the entire heart, with a particular view toward using coronary sinus drainage in studies of flow and metabolism for the entire left ventricle (9, 17). Experiments in the canine heart have demonstrated that right ventricular drainage contributes negligibly to coronary sinus outflow (6, 9, 21). The latter originates almost exclusively from left ventricular myocardium and includes 80-85% of left coronary inflow (21). The remainder of left coronary inflow represents flow to the interventricular septum, which sends 80% of its venous flow or increased slightly. The mean increment during increased afterload was from 1.7 ± 1.4% to 2.8 ± 2.0% (P < 0.05) and during increased preload was from 2.0 ± 1.3% to 3.8 ± 2.9% (0.05 < P < 0.10).

Alterations related to selective reduction of anterior descending and circumflex inflow are shown in Fig. 7. Reductions in inflow were produced by applying a screw clamp upstream to the mixing chamber in the appropriate external perfusion circuit. Flow reductions averaged 69 ± 16% in the anterior descending artery and 76 ± 15% in the circumflex artery. During restricted anterior descending inflow, GCV H2 concentration increased from 5.1 ± 3.9% to 11 ± 7.1% of CS H2 concentration (0.05 < P < 0.10). The CS He concentration decreased noticeably, from 63 ± 8.6 to 35 ± 10% of GCV He concentration (P < 0.005). During restricted circumflex inflow, GCV H2 concentration decreased from 3.7 ± 2.9% to 1.3 ± 1.4% of CS II2 concentration (P < 0.05) and CS He concentration increased from 55 ± 14% to 70 ± 17% of GCV He concentration (P < 0.005).

Interventions designed to increase anterior descending or circumflex inflow selectively are shown in Fig. 8. Prostaglandin E1, a vasodilating agent, was infused into the appropriate external perfusion circuit in a dose of

FIG. 6. Ratios of tracer concentrations before and after changes in afterload and preload. Vertical bars indicate mean values ±1 SD.

FIG. 7. Ratios of tracer concentrations before and during selective reductions in anterior descending and circumflex inflow. Format as in Fig. 6.

FIG. 8. Ratios of tracer concentrations before and during selective anterior descending and circumflex infusion of prostaglandin E1 (PGE). Format as in Fig. 6.
outflow directly into the right heart (19), and flow through the left anterior atrial artery, which sends a portion of its drainage into the left atrium (9). Thus, in the dog, coronary sinus outflow originates predominantly from the free wall of the left ventricle and is derived essentially entirely from the anterior descending and circumflex divisions of the left coronary artery. Although it has not been possible to obtain similar information in man, the postmortem injection studies of Hood (11) suggest that human coronary sinus outflow also originates predominantly from left ventricular myocardium. Septal veins connect with the coronary sinus and its tributaries to a greater degree than in the dog (20), and more than 95% of veins > 1 mm in diameter in the septum and free wall drain via the coronary sinus (11). Outflow from the posterior interventricular vein enters the coronary sinus near its right atrial ostium, regardless of whether the posterior descending artery originates from the right coronary artery or the circumflex division of the left coronary artery. Anatomical interconnections are demonstrable among virtually all venous channels (7, 12) but, as in the dog, their functional significance in the absence of gross venous obstruction has been unclear.

Information about the origin of blood sampled at various points within the coronary sinus and great cardiac vein has been limited. In a study designed to explore the feasibility of quantitating left coronary inflow from coronary sinus indicator-dilution curves for indocyanine green, Friesinger et al. (6) verified that left circumflex drainage enters the coronary sinus relatively near the coronary sinus ostium, whereas anterior descending drainage predominates in blood sampled upstream. These findings are confirmed by the data in Figs. 2 and 4. The data in Table 1 and Fig. 3 add information about the functional role of venous interconnections between geographically separate areas of the left ventricle. The prolonged period of tracer infusion assured even saturation of the anterior descending and circumflex beds by He and H2, respectively. The use of the inert gases also precluded significant recirculation of indicator. As each drained into the right atrium and was mixed with the noncoronary portion of venous return, its coronary venous concentration decreased by a factor of ~20. Because of the low solubility in blood of He and H2, a further reduction in concentration, of at least another 20-fold, occurred as each gas traversed the pulmonary circulation (14). Thus, the presence of He in blood sampled from the left marginal vein (Table 1) implies that a portion of anterior descending inflow normally reaches the coronary sinus through circumflex venous branches rather than the great cardiac vein. This conclusion is reinforced by the cooling noted in the left marginal vein after anterior descending injection of saline (Fig. 3). Although arterial as well as venous interconnections exist between the anterior descending and circumflex beds, the venous interconnections are presumed to be the functionally important ones in the present experiments. Previous studies indicate that potential arterial collateral vessels are nonfunctional prior to acute occlusion (2, 16) and that a very limited amount of arterial collateral circulation occurs after acute occlusion of either the anterior descending or circumflex artery (8). In addition, arterial injections of radioactive microspheres were employed in conjunction with venous sampling in animal 4 of Table 1; 7- to 10-μm spheres labeled with 46Sc were injected into the anterior descending artery and similar spheres labeled with 89Sr into the circumflex artery immediately after the control He and H2 measurements. Essentially 100% of these spheres are trapped in precapillary vessels (1, 4). After fixation of the heart at the completion of the experiment, full-thickness transmural sections were examined for 46Sc and 89Sr activity by conventional counting techniques (4). The 46Sc activity was localized sharply to the area perfused by the anterior descending artery, with activity in tissue adjoining the left marginal vein being <1% of activity in tissue adjoining the anterior interventricular vein. The 89Sr showed a directionally opposite distribution, with activity in tissue adjacent to the anterior interventricular vein constituting only 1–2% of activity in tissue adjacent to the left marginal vein. Thus, the anatomical venous interconnections known to exist between geographically separate areas of the canine left ventricle play a significant role in anterior descending drainage. a portion of this drainage normally reaching the coronary sinus through circumflex venous branches rather than the great cardiac vein. The findings in Table 1 and Figs. 2–8 indicate that circumflex drainage does not travel "retrograde" through the same interconnections to an appreciable degree, either under basal conditions or during a variety of physiological interventions. Normal pressure gradients within the coronary venous system would seem a reasonable basis for the functionally unidirectional nature of the interconnections.

The data in Figs. 4–8 were intended to evaluate, in a reasonably large series of animals, the origin of blood sampled in the two positions representing the greatest separation that can usually be achieved in the closed-chest situation. The data are expressed as the ratios of GCV to CS H2 concentration and CS to GCV He concentration. The GCV-to-CS H2 ratio may be thought of as an indicator of the degree to which left circumflex inflow drains into the great cardiac vein near its origin. The inability of the CS catheter to include drainage from posterior interventricular veins could cause this ratio to overestimate the fraction of circumflex outflow entering the GCV. However, the degree of overestimation is probably small, particularly if posterior interventricular drainage contains anterior descending as well as circumflex outflow. The consistently low values of the GCV-to-CS H2 ratio, both at rest and during interventions, indicate that blood sampled near the origin of the great cardiac vein remains remarkably free of circumflex outflow in a variety of physiological states. Even during severe obstruction of LAD inflow, GCV H2 averaged only 11% of CS H2, as opposed to 5% of CS H2 in the control state. Although pressure in the anterior interventricular veins was probably less than in the mar-
original veins during LAD obstruction (5), the small increment in the GCV-to-CS H$_2$O ratio may well have reflected only the reduction in LAD flow. Values for the ratio of CS to GCV He concentration can be thought of as reflecting the degree of dilution of anterior descending drainage by circumflex outflow. These ratios need to be considered not only in light of posterior interventricular venous drainage but also with regard to the contribution to GCV blood of drainage from proximal diagonal branches of the LAD, which contained neither H$_2$ nor He (Fig. 1). Postmortem injection studies indicated that these “unlabeled” segments averaged 14 ± 7% of the weight of the left ventricular free wall (excluding the septum). Their drainage no doubt often caused measured GCV He concentrations to be less than anterior interventricular vein He concentrations, thereby adding to the variability of the CS-to-GCV He ratio. Coupled with the knowledge of LAD drainage through circumflex venous branches, these limitations make it difficult to construct equivalent two- or three-compartment models of coronary venous drainage that have detailed quantitative meaning. Figures 7 and 8 do make it clear, however, that, at any given point within the coronary sinus, the fractions of sampled outflow originating from the anterior descending and circumflex arteries can change appreciably during altered physiological states. The relative contribution of anterior descending drainage decreases during selective LAD obstruction or LC vasodilation and increases during selective LC obstruction or LAD vasodilation.

On the basis of the present findings, we conclude that blood sampled near the origin of the great cardiac vein originates almost entirely from anterior descending inflow in abnormal as well as normal physiological states. Blood sampled in the coronary sinus has a more variable origin, both from animal to animal and in individual animals before and after selective changes in LAD or LC inflow. The degree of variation in the coronary sinus probably results primarily from differences in the fractions of total left coronary inflow going to the anterior descending and circumflex beds. However, it also includes any variability related to incomplete venous mixing within the coronary sinus, undetected variations in catheter position, etc. The implications of the present findings for investigations of the coronary circulation depend on which of the many aspects of coronary perfusion is being evaluated. Measurements of average flow per unit weight of myocardium with diffusable tracers should continue to give correct values when perfusion is heterogeneous, as long as even saturation is achieved throughout the tissue represented in the sampled drainage and prolonged venous-arterial differences in tracer concentration are resolved appropriately (13). Such measurements should remain accurate during interventions that accentuate the degree of heterogeneity of perfusion as long as basic patterns of venous drainage from localized segments of myocardium are not altered. On the other hand, interpretation of arterial-venous differences of “metabolic” indicators, such as oxygen or lactate, may easily be confounded by a change in the proportions of sampled outflow arising from the anterior descending and circumflex beds (3). Thus, generalizations about the limitations of regional venous sampling are difficult and, at least for the moment, individual studies must be evaluated on the basis of the particular parameters being measured.

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