Measurements of the Cardiac Output

Cardiac output (CO) is a volume of blood, pumped and transported by heart ventricles during a unit of time (generally one minute). It is same as the flow of blood through the vasculatory bed. With the exception of a short time unsettled state, both ventricles pump virtually same volume of blood. We could also say that a same volume of blood flows (in absence of pathological shunt) through the pulmonary and systemic circulation.

Physiological Cardiac Output

Minor exception to this rule is the presence of so called **physiological shunt**: A small portion of blood in the systemic circulation supplies distal bronchi. This blood returns to the heart via pulmonary veins together with oxygenated blood from alveoli, thus evading the right heart and pulmonary circulation. Therefore, to be more correct, we should say that the amount of blood passing through the left heart and systemic circulation is about 1–3% larger than the amount passing through the right heart and pulmonary circulation.

A normal value of cardiac output at rest is about **4–8 L/min**. A simple formula holds for cardiac output:

$$CO = SV \times HF \qquad (1)$$

CO—cardiac output, SV—stroke volume, HF—heart frequency. Substituting average physiological values (and converting *mL* to *L*) we can get for instance:

4,9 L/min = 70 mL/stroke × 70 strokes/min

Changes of Cardiac Output

Cardiac output can increase up to five times its resting value if needed. These changes are mostly due to the changes in heart frequency (it can go up to 180–220 strokes/min), but also due to the increase of stroke volume. Resting stroke volume varies with the phase of the respiratory cycle, because the changes of pressure inside thorax influence the venous return to the heart—it is thus advisable to measure cardiac output at the end of expirium or other fixed point (this is relevant only with the "fast methods" of cardiac output measurement).

Parameters of Cardiac Output

cardiac output depends substantially on the body size. However, it is proportional (together with many other physiological parameters) to the body surface area rather than the total body mass. We could also say that as obese individuals of given height gain weight, their mass increases faster than do their cardiac output and body surface area. It is reasonable to try to get rid of this dependence, because we want to assess purely level of cardiac performance. In order to do that we define **cardiac index** (*CI*):

$$CI = \frac{CO}{BSA} \qquad (2)$$

where BSA is body surface area computed by substituting the individual's height and weight into some of the established formulas. Nowadays, cardiac index is mostly computed automatically by the measuring device (e.g. thermodilution method apparatus) software. Cardiac index goes down in cardiac insufficiency and failure. It can also go up, for instance in the first (hypercirculatory) stage of septic shock. Other important parameter that we assess in cardiac insufficiency and failure is ejection fraction.

Among the cardiac output and cardiac index measurement procedures, there is no generally accepted gold standard method yet. Currently used methods are generally either innacurate or invasive or expensive (or combining more of the disadvantages).

Cardiac output measurement is done using following methods:

- doppler echocardiography;
- dilution methods and especially thermodilution method;
- fick's principle, traditional method;
- non-invasive modifications of Fick's method;
- other.

Doppler Echocardiography

The formula (1) is used to compute cardiac output when Doppler echocardiography is used. Heart frequency is easily measured, so it is just the stroke volume that needs to be determined. It is determined by adding up all the volume flowing across a heart valve during one cardiac cycle. The volume that flows across a heart valve in any moment (dV) is equal to the duration of the moment (dt) multiplied by velocity of blood (v) and the cross sectional area of the valve (A). The total stroke volume is a sum of volumes that crossed the valve during all the moment of one cardiac cycle. Expressed mathematically:

$$dV = A \times v \times dt = \frac{\pi\,d^2}{4} \,v\,dt \qquad (3)$$

SV = sum of all the dVs during one stroke

where d is the diameter of the valve (determined by echocardiography) and v is the velocity of blood determined by use of Doppler echocardiography (based on Doppler effect). Doppler effect is causing the frequency of the ultrasound to be higher, if the RBCs on which the ultrasound is reflected move towards the probe. Conversely, if the RBCs from which the ultrasound is reflected move away from the probe, the frequency is lower.

For math folks: The presented explication means that the stroke volume is a time integral of the flow across the aortal valve during a systole or across the mitral valve during a diastole.

Doppler echocardiography in non-invasive, cheap and relatively accurate way to measure *CO*. However, an experienced sonographist is needed.

Dilution Methods and Thermodilution Method

Using the classical method (by Stewart and Hamilton), a known amount of an indicator substance (dye, easily assessed substance, radioisotope) is injected into the venous system. Subsequently, a time course of the indicator concentration is assessed at a chosen site of the arterial tree. The distance between the aplication and measurement sites does not need to be known. The method is based (with some simplification) on the following fact: The greater the cardiac output, the greater is the velocity of blood in the vasculature and the faster is the passage of the indicator substance across the measurement site. Indicator substance should be well tolerated, well excreted and non-toxic. An example of a contrast substance is a solution of Lithium salts (e.g. Lithium Chloride); the measured quantity is then the concentration of Lithium ions Li^+.

The calculation of cardiac output is based on following formula: $$CO = \frac{n_{ind}}{\int\limits_0^\infin c_{ind}\, dt}\qquad\qquad (4)$$ where CO is cardiac output, n_{ind} the total amount of indicator substance that was injected (in moles) and c_{ind} is concentration (molarity in mol/L) of the indicator at the measurement site at a particular moment of duration dt. Mass and mass concentration (in kg/L) could be used alternatively. The integration from zero to infinity means following in practice: We measure the concentration since the application of the indicator substance up to the time point, when all the inficator passes through the measurement site (and its concentration goes back to zero) for the first! time. Formula (4) could be understood the following way: If there were no dilution of the indicator substance between the injection site and the measurement site down the stream, then the greater the cardiac output, the faster the indicator passes throuh the measurement site. The value of the integral is smaller in such a case (the total sum of dt is smaller) and hence the cardiac output comes out greater (we divide by a greater number of the integral). In case of the indicator being mixed and diluted lenghwise during the time interval between the aplication and measurement (which is going to happen, for sure), the result will remain unchanged. This is because the indicator concentration (c_{Ind}) decreases with dilution, but simultaneously the time of indicator passage dt increases - and the value of integral stays constant. There is also a possibility of the indicator being diluted crosswise, for instance due to the fact of the increase in cross sectional area of the vasculatory bed at the measurement site. Think this situation through to see that this situation also does not change the value of the integral (or one integration step). Hint: An increase of cross sectional area causes a decrease in rate of flow.

where CO is cardiac output, n_{ind} the total amount of indicator substance that was injected (in moles) and c_{ind} is concentration (molarity in mol/L) of the indicator at the measurement site at a particular moment of duration dt. Mass and mass concentration (in kg/L) could be used alternatively. The integration from zero to infinity means following in practice: We measure the concentration since the application of the indicator substance up to the time point, when all the inficator passes through the measurement site (and its concentration goes back to zero) for the first! time. Formula (4) could be understood the following way: If there were no dilution of the indicator substance between the injection site and the measurement site down the stream, then the greater the cardiac output, the faster the indicator passes throuh the measurement site. The value of the integral is smaller in such a case (the total sum of dt is smaller) and hence the cardiac output comes out greater (we divide by a greater number of the integral). In case of the indicator being mixed and diluted lenghwise during the time interval between the aplication and measurement (which is going to happen, for sure), the result will remain unchanged. This is because the indicator concentration (c_{Ind}) decreases with dilution, but simultaneously the time of indicator passage dt increases - and the value of integral stays constant. There is also a possibility of the indicator being diluted crosswise, for instance due to the fact of the increase in cross sectional area of the vasculatory bed at the measurement site. Think this situation through to see that this situation also does not change the value of the integral (or one integration step). Hint: An increase of cross sectional area causes a decrease in rate of flow.

Thermodilution Method

Thermodilution method is a loose modification of the classical method. The CO is measured by use of *Swan Ganz catheter*. The applied indicator is heat (or as a matter of fact cold), because the injected substance is a saline solution (a bolus of e.g. 20 mL) at temperature of 0 °C. The sensor placed at the end of the catheter simply measures temperature. The sensor is placed at a known distance (for instance 18 cm) down the stream from the application site.

Contrary to the classical method, it is necessary to know the distance between the application and measurement sites, because the heat (cold) dissipates freely out of the vasculatory bed (the tissue surrounding the vessel gets colder as well). Hence, the formula (5), which is valid for the classical method, can only be used with certain reservation.

Measurement principle: If the cardiac output is high, the cold will reach the measurement site fast and it will be less diluted (the decrease of temperature will be significant and the subsequent return back to normal will be fast). On the other hand, if the cardiac output is low, then it will take longer before the heat reaches the measurement site and after this time the cold will already be diluted (the decrease of temperature will be mild and the return back to norm will be gradual). A calibration of the method (finding out which cause of temperature change corresponds to which cardiac output) has been done by simultaneous use of other methods. Thermodilution method is **invasive, yet it is used relatively often**. The accuracy is not perfect, thus several consequent measurements (saline bolus applications) are generally used and the average is taken as a result.

Fick principle and the classic method based on it

Note: We will refer to blood entering lungs by pulmonary arteries as venous in this section. The blood leaving lungs by pulmonary veins and flowing into systemic arteries will be referred to as arterial blood

Fick principle is a straightforward application of the law of mass conservation. The amount of oxygen entering lungs by venous blood plus the amount extracted from the breathed air has to be equal the amount of O_2 leaving lungs by arterial blood. Said alternatively: **The difference between the (substance) amount of oxygen leaving lungs by arterial blood during one minute and the amount entering lungs by venous blood during same time is equal the amount of O_2 extracted from the breathed air**. Expressed by a formula:

$$Q_{O_{2}Art} - Q_{O_{2}Ven} = Q_{O_{2}Air} \qquad\qquad\qquad (5)$$

where Q_{O2Art} is the substance amount of oxygen leaving in arterial blood (in mol/min), Q_{O2Ven} represents the amount coming by the venous blood and Q_{O2Air} amount coming by air.

The (substance) amount of O_2 coming and leaving by blood can be expressed as product of cardiac output and molar concentration of oxygen in venous and arterial blood, respectively (in mol/L):

$$Q_{O_{2}Ven} = CO \times c_{O_{2}Ven} \qquad\qquad\qquad (6)$$

$$Q_{O_{2}Art} = CO \times c_{O_{2}Art} \qquad\qquad\qquad (7)$$

Substituting into formula (5), we get:

$$SV \times \left(c_{O_{2}Art} - c_{O_{2}Ven} \right)= Q_{O_{2}Air} \qquad \qquad (8)$$

Hence, cardiac output can be computed as:

$$CO = \frac{Q_{O_{2}Air}}{c_{O_{2}Art} - c_{O_{2}Ven}} \qquad \qquad \qquad (9)$$

We have used flows of the substance amount of oxygen (in mol/min) during the derivation of the formula for cardiac output. Alternativelly, we could have used the flows of mass of oxygen (in g/min). Sometimes, flows of volume of oxygen considered in gas phase (under constant pressure and temperature) are used. Although the volume of oxygen extracted from the breathing mixture is expressed naturally in mL/min, it is rather awkward to express the coming and leaving of oxygen by blood in mL O_2/min. This expression wants to say that we consider the volume of oxygen coming and leaving by blood as if it were in gas phase (under constant pressure and temperature).

Carrying out the measurement: The amount of oxygen used from the breathing mixture in one minute (Q_{O2Air}) can be measured by patient breathing into a closed bag for some time. The CO_2 leaving the body is absorbed in the bag and the extraction of O_2 from the gas mixture will manifest as decrease od bag volume. Change of volume is then recalculated into the corresponding amount of substance of oxygen. Concentration of oxygen in mixed venous blood is assessed by measuring pO_2 in mixed venous blood - **cathetrisation of central veins by Swan Ganz catheter is thus necessary**. Concentration of O_2 in arterial blood is assessed by **drawing arterial blood** (generally from radial artery) and measuring pO_2 in it. Even though this classical method is quite accurate, it is invasive and rarely used.

Modern non-invasive modifications of Fick's method

Fick principle (law of mass conservation) can be used with other substances than oxygen. For instance: CO_2 entering lungs by venous blood minus the amount leaving by arterial blood is equal to the amount exhaled to the air. Alias:

$$Q_{CO_{2}Ven} - Q_{CO_{2}Art} = Q_{CO_{2}Air} \qquad \qquad (10)$$

A formula for computing cardiac output CO based on the measurement of CO_2 is obtained by rearrangement of (10):

$$CO = \frac{Q_{CO_{2}Air}}{c_{CO_{2}Ven} - c_{CO_{2}Art}} \qquad \qquad (11)$$

Non-invasive measurement of arterial blood gases: In order to find out the arterial concentration of blood gases, we need to know arterial pO_2 or pCO_2. An interesting option of non-invasive measurement of these partial pressures is represented by so called **"end – tidal" pO_2 or end-tidal pCO_2**. The measured quantity is pO_2 or pCO_2 in the expired air at the end of deep expiration. It is supposed that the end expiratory air is coming completely from alveoli and thus has the same pO_2 and pCO_2 as the blood leaving these alveoli. This method can bypass the necessity of collecting arterial blood. Unfortunately, the method fails in presence of badly ventilated parts of lungs (as seen atelectasis or obstruction). The badly ventilated part of lungs can, of cause, become even pathological shunt in extreme cases (as seen in ARDS).

Non-invasive measurement of venous blood gases: A method called **rebreathing** can be used to measure especially the venous pCO_2. It consists of a repeated breathing into a bag with gas mixture (for no more then 45 seconds) up to the point, when pCO_2 inside the bag does not change anymore. This steady state appears when the pCO_2 inside the bag equals the venous pCO_2 – thus, we simply measure the pCO_2 inside the bag. This procedure overcomes the necessity of troublesome cathetrization of central veins.

Use of other gases than O_2 and CO_2: Fick priciple was modified even for use with more exotic gases than oxygen and carbon dioxide. The measurement procedes as follows: The patient starts to breath a mixture containing the used substance. Afterwards, the concentration (partial pressure) of this substance in arterial blood is measured. Venous concentration of a substance not normally present in air is zero, so its venous inflow into lungs is also zero before we start the measurement. This fact can be taken advantage of and the equation (5) reduces to:

$$Q_{exot\,Art} = Q_{ exot\,Air} \qquad \qquad (12)$$

After some rearrangements, cardiac output can be computed as:

$$CO = \frac{Q_{ exot\,Air}}{c_{ exot\,Art}} \qquad \qquad (13)$$

where $c_{exot\ Art}$ is the (molar) concentration of the exotic gas in arterial blood(in mol/l) and $Q_{exot\ Air}$ is the rate of uptake of this gas from the breathing mixture (v mol/min). This method also bypasses the necessity of central venous cathetrization.

Summary: Non-invasive and less invasive methods based on the Fick principle have a potential to become accurate and inexpensive procedures of measuring cardiac output. Possibly, other gases than O_2 a CO_2 can be the choice. Eventual use of oxygen or carbon dioxide has still to overcome many problems: The accuracy of conversion of partial pressures into concentations, where even things like pH can play a role, mutual interactions of the two gases and hemoglobin etc. Also, the non-homogenity of lungs can cause problems.

Other methods

Magnetic resonance: Resonance properties of protons in the nucleus do change with respect to velocity. Thus, magnetic resonance can be used as an *accurate* way to measure the flow in aorta (cardiac output). The method is *expensive*, it is only used in research.

Mathematical analysis of pulse pressure wave: The shape and amplitude of the pulse pressure wave (the way the pressure changes in an artery from systolic to diastolic and back) varies with the cardiac output. Pulse pressure wave is measured either using the standard pressure cuff or a sensor which sticks to the skin above an artery. Mathematical analysis of this wave can reveal the value of cardiac output. However, the pulse pressure wave also depends substantially on the properties of arteries, this being the problematic spot of the method. For instance, elderly people often lose elasticity of aorta. Consequently, it does not accomodate all the

stroke volume well and the systolic pressure increases while diastolic pressure stays normal. The pulse pressure analysis method might be useful after calibration for the given individual done by other methods. It could help in non-invasive continous monitoring of cardiac output.

Impedance cardiography (measuring electrical resistance of the chest): Electrical resistance of chest can be measured using only few electrodes. The resistance changes during the cardiac cycle due to the changes of the volume of blood inside the heart. These changes can be used for calculation of stroke volume and consequently cardiac output. The method is nonexpensive and non-invasive, but not accurate.

Links

Related articles

- Cardiac Output