BVM - Blood Volume Monitor
Improved blood pressure stability with blood volume controlled ultrafiltration
Intradialytic complications – still a problem today?

Symptomatic hypotension is one of the most frequent problems encountered during haemodialysis treatment. The symptoms of this undesirable intradialytic effect are usually rapid falls in blood pressure, frequently accompanied by cramps, sometimes nausea, dizziness, headache and vomiting: in rare cases, the patient may even lose consciousness (Fig. 1).

The necessary measures, such as reduction of the ultrafiltration rate or infusion of saline solution, are often detrimental to the required aim of dehydration of the patient, and prevent the specified dry weight being reached. A repeated reduction of the ultrafiltration rate or even premature discontinuation of dialysis may be necessary because of hypotensive episodes, the required dialysis dose may not be achieved.

In addition to the acute distress experienced by the patient, symptomatic hypotension can have adverse effects on long term health. Many studies have demonstrated the negative consequences of hypotensive episodes. Evidence has been found that these are associated with reduced oxygen supply, damage to cardiac and cerebral tissue, accelerated loss of residual renal function and an increase in morbidity and mortality [1, 2].

Intradialytic complications are still a problem.

Which patients experience hypotensive episodes during dialysis?

The excess fluid, which has accumulated in a patient in the 2 - 3 days between each treatment, is withdrawn by means of ultrafiltration during haemodialysis and, as a result, the volume of blood in the patient is reduced. The ability of the body to compensate for such rapid changes in blood volume and to maintain blood pressure within an acceptable range differs greatly from patient to patient. These compensatory mechanisms are apparently overstrained in those patients who frequently experience hypotensive episodes: this is particularly the case in older patients and patients with pre-existing cardiovascular problems.

It has been established that the patients who are frequently more sensitive to a reduction of relative blood volume during ultrafiltration are more commonly found among the following groups [4]:

- Elderly patients
- Patients with generally low ultrafiltration volume
- Patients with generally low diastolic blood pressure at the beginning of dialysis
- Patients with a history of myocardial insufficiency and/or cardiac arrhythmia.

Despite medical and technological improvements, the size of this group of problem patients has not diminished as patients are becoming increasingly older and, not infrequently, have several comorbid diseases which complicate treatment.
Why does symptomatic hypotension occur?

Fifty to sixty percent of the human body consists of water, 55% of which is found in the cells and approximately 45% in the extracellular space. About 5% of the body weight is due to the blood plasma.

The fluid, which has accumulated in the body of a dialysis patient in the treatment-free interval, is withdrawn in the few hours of the dialysis treatment. This leads to fluid displacement and temporary imbalance between the various fluid compartments. Moreover, ultrafiltration influences one of the smallest fluid compartments of the human body – the blood plasma. Ultrafiltration and the accompanying plasma refilling from the surrounding tissue have a significant effect on blood volume.

Assuming that the ultrafiltration rate corresponds exactly to the refilling rate, fluid inflow from tissues and fluid removal would be equivalent and the blood volume would remain unchanged. An almost constant blood volume is sometimes observed in overhydrated patients: the volume removed by ultrafiltration is immediately replaced by fluid from the surrounding tissue in such cases [5, 6].

As a rule, however, there is a progressive reduction of blood volume because there is only a limited volume of excess fluid in the body and the inflow of fluid into the blood plasma decreases as the dry weight of the patient is approached.

Blood volume and blood pressure are closely linked [7, 8]. If cardiac output and the status of blood vessels were unchanged, a reduction in blood volume would lead to reduced blood pressure. The complex regulatory mechanisms used by the body to control blood pressure ensure, however, that there is at least partial compensation of any reduction in blood volume by means of e.g. a reduction of the diameter of blood vessels (vasoconstriction) so that the blood pressure of the patient is maintained within an acceptable range. If these compensatory mechanisms fail, symptomatic hypotension results.

There are a large number of factors which influence symptomatic hypotension. A wide range of physiological parameters significant for cardiovascular stability are altered during haemodialysis treatment: dialysis, for example, has effects on body temperature and plasma osmolarity.

One of the most important factors influencing the blood pressure control system of a patient is the reduction of blood volume caused by ultrafiltration during haemodialysis treatment. Without ultrafiltration symptomatic hypotension is observed only in rare cases. During dialysis treatments with ultrafiltration, hypotensive episodes most commonly occur during the second half of the treatment, particularly towards the end of the session when patients approach their dry weight (see also Fig. 13) [9, 10].
One of the main causes of symptomatic hypotension would thus appear to be an ultrafiltration rate which is not appropriately adjusted to the current patient status: more fluid is withdrawn from the circulating blood than can be supplied from the surrounding tissue: blood volume falls rapidly (Fig. 4).

Often hypovolaemia due to an inadequate ultrafiltration rate is a reason for hypotensive episodes, mostly towards the end of the haemodialysis session, when patients approach their dry weight.

What reduction of blood volume can patients tolerate?

Many of the factors in Fig. 3 influence symptomatic hypotension via the blood volume. Measurement of blood volume using the Fresenius Medical Care 4008 blood volume monitor (BVM) can provide information on whether there is still excess water in the patient’s body, whether this fluid is being used to refill blood vessels and there is adequate refilling and whether the physiological regulatory mechanisms, such as the contraction of blood vessels, are sufficient for compensation.

The BVM determines the relative blood volume (RBV) of the patient: the value at start of haemodialysis is automatically set to 100 % and all changes are registered relative to this initial value.

With the BVM, it is possible to monitor the changes in blood volume which occur during a haemodialysis treatment: the current RBV is shown on the display of the BVM module while the changes in RBV during the on-going treatment can be followed on the screen of the 4008H/S dialysis machine (Fig. 5).
Although there are differences in the extent of overhydration from treatment to treatment in nearly all cases, most patients tend to exhibit an individual and specific profile of reduction of relative blood volume during treatment.

While some patients experience hypotensive episodes after only relatively small reductions of 5 – 10 % in blood volume, the blood pressure of other patients remains stable even after reductions of blood volume of up to 29 % (Figs. 6, 7). [4, 9, 10]

The critical relative blood volume (RBV_{crit}) represents the limit at which hypotensive episodes become more frequent in the individual patient.

Once the critical RBV for a particular patient has been identified, the RBV_{crit} value can be used for automatic control of the ultrafiltration rate using the BVM.

The BVM regulates ultrafiltration rate on the basis of the current RBV to ensure that if the RBV_{crit} value is approached, the ultrafiltration rate is reduced and the RBV does not fall below the critical limit.

The tolerance to blood volume reduction differs from patient to patient.
How does the BVM work?

Ultrafiltration removes fluid from the body of the patient during dialysis. The volume of plasma water is reduced during ultrafiltration (it can pass through the capillary membrane and the dialyser membrane), but certain blood constituents (cells, haemoglobin, plasma proteins) are unable to leave the intravascular space. The intravascular protein mass thus remains largely constant even when there are changes in blood volume due to ultrafiltration or refilling [17]. The result is a change to the relative mass profile and concentration of proteins and thus to the density of the monitored blood.

Changes in the density of a medium can be easily determined by measuring the velocity of sound in the medium. While sound travels slower in a less dense medium, its velocity increases with density so that, for example, sound travels five times faster in water than in air. The BVM is able to determine the density of blood very accurately by using an ultrasonic measuring technique.

As an example, the increase in concentration, which accompanies a reduction of blood volume from 5 to 4 litres, is shown in Figure 8.

Blood volume is measured in a special cuvette placed in the arterial blood line. As temperature also influences the velocity of sound, this is also measured and taken into account in the calculation. A transmitter emits short ultrasonic impulses which are registered by a receiver mounted on the opposite side of the cuvette. The illustration provides a scheme of the cuvette and the sensor head of the blood volume monitor (Fig. 9).

The transit time of the ultrasonic pulse is determined on the basis of the emitted and received signal and this is used to determine the velocity of sound in the blood. This precise timing method allows the relative blood volume to be measured with an accuracy of better than 2 % [19]. The quicker the passage of the pulse, the denser the blood between transmitter and receiver and the lower the relative blood volume of the patient.

In addition to measuring and displaying blood volume without influencing the on-going treatment, the blood volume monitor can also use the results of continuous monitoring of blood volume to automatically adjust the ultrafiltration rate.

The BVM is a non-invasive and accurate automatic tool to monitor blood volume.
How does the blood volume monitor regulate the ultrafiltration rate?

The results of continuous measurement of RBV can be used to ensure that the reduction of blood volume is restricted to a level which is tolerable for the individual patient. After the critical relative blood volume (RBVcrit) for the patient has been entered in the instrument and the blood volume monitor has been started, the rate of ultrafiltration is appropriately adjusted to the actual blood volume to ensure that the RBV value does not fall below the critical limit for the patient.

The blood volume of the patient at start of treatment is, per definition, 100%. The critical blood volume for the patient is entered in the BVM at the start of treatment. When blood volume regulation starts, the relative blood volume is automatically divided into three zones, whereby the range between baseline (100 %) and the individual critical blood volume (RBVcrit) is halved.

Green zone:
(Non-critical range: no regulation by the BVM) The patient is overhydrated at the beginning of the treatment session: for this reason the initial UF rate is high (twice the mean UF rate), but this is continuously reduced throughout the treatment.

Yellow zone:
(Regulation required: the BVM prevents a fall in RBV to the critical blood volume range) The blood volume of the patient approaches the individual RBVcrit; the nearer the blood volume comes to the RBVcrit, the more the UF rate is reduced. When RBV increases, UF rate is correspondingly increased.

Red zone:
(Critical range: there is a high probability of blood volume-related hypotensive episodes) Ultrafiltration rate is reduced to a minimum (100 mL/h) if blood volume falls below the RBVcrit.

An example:
It is intended to remove 4 litres within 4 hours from a patient by means of UF (mean UF rate: 1,000 mL/h): the critical relative blood volume (RBVcrit) for the patient is 85%.

The initial UF rate in the green zone (100 – 92.5 %) is twice the required mean UF rate (i.e. 2,000 mL/h). This rate is linearly reduced (e.g. to 1,500 mL/h after 1 hour, to 1,000 mL/h after 2 hours, to 500 mL/h after 3 hours). If RBV falls below 92.5 % and enters the yellow zone, RBV-dependent regulation commences: the closer RBV approaches RBVcrit, the lower the UF rate becomes. In most cases, this reduction of the UF rate is sufficient to prevent any further fall in RBV. If, however, the critical limit is reached and RBV enters the red zone below 85 %, UF is continued at a minimal rate only. If RBV subsequently increases, the UF rate is also correspondingly increased.

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Shown are the examples of two treatments conducted with BVM regulation in the same patient with an RBVcrit of 85 % [14]. While RBV remained in the green zone during the first treatment and there was a linear reduction of UF rate over the duration of dialysis, RBV fell to the yellow zone during the second treatment and the UF rate was thus appropriately adjusted to ensure that RBV did not fall below the RBVcrit (Fig. 10).
**Critical RBV - an individual value**

Critical RBV is an individual value that can differ considerably from patient to patient. In a clinical study, the individual RBV\text{crit} values determined for 60 patients with unstable cardiovascular status were found to be in the range from baseline 100 % to 71 %: the mean RBV\text{crit} of all patients was approximately 88 %.

**Gradual determination of critical RBV**

In cases in which it is considered advisable to commence with BVM as soon as possible, a mean value of 88 % (the value determined in a population of dialysis patients with frequent intradialytic hypotension) can be assumed for the critical RBV. In subsequent treatments, this initial value can be adjusted, if necessary, in 1 – 2 % steps until the individual RBV\text{crit} value is determined:

- If hypotensive episodes occur during treatment, a higher value for RBV\text{crit} should be set for the next treatment.

- If the BVM displays the message that the UF target will not be achieved within the given duration of treatment (“BVM: UF target???”), a lower value for RBV\text{crit} should be used for the next treatment.

**The determination of critical RBV in several treatments**

The safest way to determine individual RBV\text{crit} is to conduct several treatments without active regulation, but using the BVM to register RBV: the mean of the limit values for RBV (RBV during hypotensive episodes or the minimum RBV during treatment) can then be used as the value for RBV\text{crit}, nevertheless it may be subsequently necessary to conduct fine adjustment of this value in steps of 1 %.

**Note:**

A high value for RBV\text{crit} has been observed in elderly patients, patients with generally low ultrafiltration volume, patients with low pre-dialytic diastolic blood pressure, and patients with myocardial insufficiency and/or cardiac arrhythmia.

In the example shown in Fig. 10, RBV was in the green zone in the first 30 minutes. The rapid fall in RBV was countered by a reduction in ultrafiltration rate and after approximately 1 hour RBV stabilised in the yellow zone as a result of adjustment of the ultrafiltration rate to the range 87 – 90 %. The changes in RBV during on-going blood volume regulation are displayed on the screen of the 4008 haemodialysis machine (Fig. 11).

**By BV control the ultrafiltration rate is adjusted automatically according to the individual relative blood volume limit of each patient.**

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**How is the critical relative blood volume (RBV\text{crit}) determined?**

**Fig. 11: RBV during a BV controlled treatment in the display of the 4008 dialysis machine**

![Fig. 11: RBV during a BV controlled treatment in the display of the 4008 dialysis machine](image-url)
What are the clinical benefits of regulation of the UF rate using the BVM?

The regulation of the ultrafiltration rate on the basis of blood volume results in a significant reduction of the frequency of hypotensive episodes. In a multicentre study, in which alternate phases of haemodialysis treatment without regulation and phases of haemodialysis treatment with blood volume-dependent control of UF rates were compared, a marked reduction of adverse intradialytic events was observed as a result of regulation. In 27 patients with frequent hypotensive episodes, 886 hypotensive episodes were registered during 1,170 haemodialysis treatments.

The mean frequency of hypotensive episodes per treatment fell markedly when blood volume regulation was used (Fig. 12) [15].

Of particular interest was the time point at which hypotensive episodes occurred during treatment. It was already known from a previous clinical study that the frequency of hypotensive episodes increases during treatment if the UF rate remains constant, and that the frequency towards the end of a session is up to ten times higher than at the start of treatment [4, 9, 10, 15].

Blood volume-dependent control prevented the marked increase in frequency of hypotensive episodes during the second half of treatment. Moreover, the number of hypotensive episodes during the first part of treatment was not greater than with a constant UF rate, despite the fact that the mean UF rate was twice as high during this period (Fig. 13) [15].

Due to the automatic regulation of the ultrafiltration rate less hypotensive episodes were observed, especially in the second half of the haemodialysis session.

Fig. 12: Reduction of frequency of hypotensive episodes with blood volume controlled UF

Fig. 13: Hypotensive episodes are mainly reduced in the second part of the haemodialysis treatment
Operation of the BVM

The Fresenius Medical Care blood volume monitor is easy to operate. When setting up the haemodialysis machine, the cuvette of the arterial blood line should be inserted into the blood volume monitor.

Calibration of the BVM is performed automatically. Calibration is essential if the BVM is used to regulate blood volume.

Once the individual critical relative blood volume (RBVcrit) value for the patient has been entered, blood volume control is initiated by the push of a button. The currently measured value for relative blood volume is shown in the display of the BVM (Fig. 14); the changes in relative blood volume over time can be followed on the screen.

Operation of the machine is described in detail in the operator’s manual.
If overhydration is more severe than usual, is it advisable to change the customary RBV\textsubscript{crit} value for a particular patient?

No. There is little change to the blood volume in a patient with severe overhydration as the excess fluid in the body leads to a high rate of refilling and the relative blood volume remains close to the baseline of 100\% for a longer period. There is thus no benefit during the first phase of a haemodialysis treatment if the individual RBV\textsubscript{crit} is changed, while there is actually the risk in the last phase of a treatment that either the patient will be inadequately protected against hypotensive episodes (marked fall in blood volume and occurrence of hypotensive episodes because RBV\textsubscript{crit} is too low) or that the UF target will not be achieved (“BVM : UF target???” RBV\textsubscript{crit} is possibly too high).

Does the high ultrafiltration rate at the beginning of blood-volume controlled dialysis treatment lead to complications in patients?

Not in most cases. As a rule, patients are overhydrated at start of dialysis and can usually tolerate an initially high ultrafiltration rate.

Very few hypotensive episodes occur at the beginning of treatment with a constant ultrafiltration rate (as in the standard method), but these occur more frequently towards the end of treatment.

Treatment commences at double the mean required UF rate when the BVM control is used, but this is progressively reduced over time assuming that the continuously measured relative blood volume (RBV) does not approach the individual RBV\textsubscript{crit} for the patient (i.e., remains in the green zone as in Fig. 5). If RBV approaches the individual RBV\textsubscript{crit} (yellow zone as in Fig. 5), the ultrafiltration rate is further reduced.

For the few patients who do not tolerate a high ultrafiltration rate in the early stages of treatment, the maximum ultrafiltration rate can be restricted by entering an appropriate value for the parameter UFR\textsubscript{max} at the beginning of blood volume-regulated treatment.

Is it possible to stop regulation by the BVM during an on-going treatment?

Yes. BVM control of ultrafiltration can be terminated at any time. To discontinue BVM regulation, press the UF control button. The 4008 haemodialysis machine then automatically calculates the mean UF rate required to achieve the UF target within the time remaining for treatment. The treatment is then continued at this constant rate as in standard haemodialysis. Treatment can be continued at this UF rate, or the BVM regulation can again be initiated. It should be noted, however, that without active regulation by the BVM, there is no limiting RBV\textsubscript{crit} value, so that there is the risk of symptomatic hypotension.

Can machine settings be altered during an on-going blood-volume regulated treatment?

Yes. Settings can be altered during on-going treatment. Smaller adjustments to dialysis duration or the UF target can even be of benefit if the machine has displayed the “BVM: UF target???” message and one wishes to continue with BVM-controlled treatment. Of course, an adjustment of the set RBV\textsubscript{crit} value can also be advisable during dialysis if it becomes apparent shortly after commencement of treatment that the wrong value has been entered. Adjustment of the RBV\textsubscript{crit} value during the last third of a haemodialysis treatment is rarely of any benefit.
Can patients eat and drink during dialysis?

Nutritional intake during haemodialysis is not infrequently associated with hypotensive episodes. It would seem that some patients are particularly prone to this adverse effect immediately after eating or drinking [16, 17]. It is thus advisable that sensitive patients avoid eating or drinking during dialysis (e.g. by ensuring that they take meals prior to treatment) or that substantial meals are replaced by more frequently taken small snacks.

When relative blood volume is measured during nutritional intake, it is frequently observed that relative blood volume can temporarily fall by several percent. In sensitive patients, a reduction in this range can be sufficient to trigger a hypotensive episode. Blood volume control takes into account any transient reduction of blood volume and reduces the risk of hypotension by reducing the UF rate if the relative blood volume approaches the individual RBVcrit value.

During blood volume-controlled haemodialysis treatment, the machine displays the message “BVM: UF target ????”. What steps should be taken?

The warning message “BVM: UF target ????” is displayed on the screen if it appears unlikely that the specified UF target will be achieved within the time remaining. When this warning message is displayed, the regulation of ultrafiltration by the BVM is automatically terminated.

If the RBVcrit value for the patient has been accurately determined over several treatments, this message should appear only rarely and within the last hour of treatment, if at all.

The following measures are recommended if the message is displayed:

- Assuming this is possible, the duration of treatment can be prolonged: it is often possible to achieve the UF target with active regulation of treatment even with a prolongation of only 10 minutes. Try increasing the UF duration slightly, switch on UF again and restart the BVM.

- Assuming this is possible, the ultrafiltration target can be reduced: it may be possible, for example, that 100 mL volume of fluid which is not withdrawn during the on-going treatment can be easily withdrawn during the next treatment when the cardiovascular stability of the patient may have improved. Try reducing the UF target slightly, switch on UF again and restart the BVM.

- If neither of the above options is possible, switch on UF again and allow the 4008 dialysis machine to calculate the required UF without active regulation. In this case, the dialysis machine will withdraw the specified volume from the patient, but the ultrafiltration rate will not be adjusted to account for any falls in blood volume. Please note that the patient can be particularly sensitive to rapid reduction of blood volume during the latter phases of treatment.

If the warning “BVM: UF target ????” is displayed during several treatments without occurrence of hypotensive episodes, it is advisable to adjust RBVcrit: i.e. reduce the value by 1% for the next treatment.

If the individual RBVcrit for a patient has been determined on the basis of only a few treatments, it is possible that the message will be displayed before the last quarter of the treatment; this probably means the value for RBVcrit entered on commencement of treatment was too high. In this case, the following measures are recommended:

- Restart ultrafiltration only and allow the 4008 dialysis machine to calculate the required UF rate without active regulation. Set RBVcrit to a value which is 2% lower at the next treatment with active BVM regulation.
References


