



Zero reference level for right heart catheterisation

Gabor Kovacs, Alexander Avian, Andrea Olschewski and Horst Olschewski

Affiliations: Ludwig Boltzmann Institute for Lung Vascular Research, Graz, and Medical University of Graz, Graz, Austria.

Correspondence: G. Kovacs, Ludwig Boltzmann Institute for Lung Vascular Research, 8010 Graz, Stiftingtalstrasse 24, Austria. E-mail: gabor.kovacs@klinikum-graz.at

ABSTRACT Although in the pulmonary circulation small pressure differences may alter the categorisation of patients, there is no consensus on a standard zero reference level (ZRL). In the supine position, ZRL is mostly set at “5 cm below anterior thorax surface”, “1/3 thoracic diameter below anterior thorax surface”, “mid-thoracic level” or “10 cm above table level”.

We retrospectively assessed the distance of these four ZRLs from computed tomography-derived right and left atrial centre levels and from one another in patients undergoing right heart catheterisation and calculated the respective differences in pressure readings.

We included 196 consecutive patients. The ZRL at “1/3 thoracic diameter” was most often (98.5%) level with the right atrium, and the ZRL at “mid-thoracic level” was level with the left atrium (97.4%), revealing a median (range) pressure difference of -0.3 (-3.0–1.3) and 0.2 (-2.0–1.3) mmHg from the right and left atrial centre level, respectively. The largest differences (8.0 (2.0–15.4) mmHg) were found between the ZRLs “5 cm below anterior thorax surface” and “10 cm above table level”. Accordingly, 59% *versus* 80% of patients would be classified with pulmonary hypertension and 7% *versus* 38% with elevated left heart pressures.

The choice of ZRL strongly influences pulmonary pressure readings and pulmonary hypertension classification. 1/3 thoracic diameter mostly represents the right atrium while the left atrium is best represented by the mid-thoracic level.



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Introduction

Right heart catheterisation is the gold standard for the diagnosis of pulmonary hypertension (PH). It allows the direct assessment of pulmonary arterial pressures (PAP), pulmonary arterial wedge pressure (PAWP) and right atrial pressure (RAP), as well as cardiac output. All these measurements are of great importance for the diagnosis, classification and prognostic assessment of PH [1]. Diagnostic and therapeutic strategies largely depend on determining whether the mean PAP (mPAP) and PAWP exceed 25 mmHg and 15 mmHg, respectively. Although all invasive pressure readings rely on the comparison with a zero reference level (ZRL), there is a lack of standardisation for the ZRL during catheterisation [1, 2]. This may lead to considerable differences in pressure readings [3, 4], with each centimetre difference between ZRLs causing a pressure difference of 0.78 mmHg. According to the published literature, the ZRL is generally recommended to be set at the level of the right atrium, or at the level of the tricuspid valve, based on the concept of the “hydrostatic indifferent point” representing a location in the circulatory system at which gravitational pressure factors caused by changes in body position do not much affect the pressure measurements [5]. In practice, the most frequently used ZRLs in the supine patient are at 5 cm below the anterior thorax surface [6], at 1/3 of the thoracic diameter below the anterior thorax surface [7], at the mid-thoracic level [8] and 10 cm above table level [9]. Nevertheless, there are also arguments for setting the ZRL at the level of the left atrium, particularly if left heart pressures and the distinction between pre- and post-capillary PH are the focus of interest. Although it may be argued that some methods may be more suitable for right heart haemodynamics and others for left heart haemodynamics, and that the cardiac anatomy may be changed due to the specific disease, a general consensus on the ZRL would be most important. The goal of this study was to compare the most frequently used ZRLs with the anatomical position of the right and the left atrium, as derived from computed tomography (CT) scans in patients admitted for right heart catheterisation. We found that ZRL has a very important impact on the diagnosis and classification of PH.

Patients and methods

In this retrospective study, we included all consecutive patients who were referred to our PH clinic for right heart catheterisation between 2006 and 2011, and also had subsequent chest CT. All examinations were performed at the Medical University of Graz, Graz, Austria by an experienced medical team. CT examinations were performed on a 128 slice CT system (Siemens Solutions, Erlangen, Germany). The CT section including the tricuspid valve and optimised for the right atrium was used for further analysis in each patient. In the CT images, in every patient the distance between the anterior thorax surface above the sternum (the skin above the sternum) and the anterior wall of the right atrium (fig. 1a), the diameter of the right atrium (fig. 1b) and the distance between the table level and the posterior wall of the right atrium (fig. 1c), as well as the distance between the middle of the right atrium and the anterior thorax surface (fig. 1d) and table level (fig. 1e) was measured. The centre of the right atrium was chosen as reference ZRL. The distance of the four most frequently used ZRLs (5 cm below the anterior thorax surface; 1/3 thoracic diameter below the anterior thorax surface; mid-thoracic level; 10 cm above table level) from the reference ZRL and from one another were calculated in each patient. Pressure differences (mmHg) were derived from the measured distances between ZRLs using the following equation: pressure difference (mmHg) = 0.78 × distance (cm). The CT scans were reviewed by two independent reviewers and discrepancies in measurements were decided by consensus.

For the comparison of ZRLs with the anatomical position of the left atrium, the CT section optimised for the left atrium was used in analogy to the method described for the right atrium. The axial localisation of the right and left atrium corresponded in most cases to the insertion of the fourth or fifth rib anteriorly to the body of sternum.

Our centre-specific method of defining the ZRL was the level of the anterior axillary line. According to earlier studies, in most cases this corresponds to a ZRL at 1/3 thoracic diameter [10].

Data are presented as mean ± SD or as median (range). If the assumption of normally distributed data was met, the measures of PH and non-PH patients were compared by two-sided t-test. Otherwise, nonparametric tests (Mann–Whitney U-test) were used. The correlation between thoracic diameter and other parameters was examined by Pearson or Spearman correlation. p-values <0.05 were considered significant. For data analysis, SPSS 19.0.0 (SPSS Inc. Chicago, IL, USA, 2011) was used.

Results

We included 196 consecutive patients (n=46 pulmonary arterial hypertension, n=19 PH due to left heart disease, n=33 PH due to lung disease, n=29 chronic thromboembolic PH, n=8 other PH and n=61 patients without PH) in this study (patient characteristics in table 1). The intrathoracic distances, as defined in figure 1, are represented in table 2 for both the right and left atrium. The right atrium was larger in PH

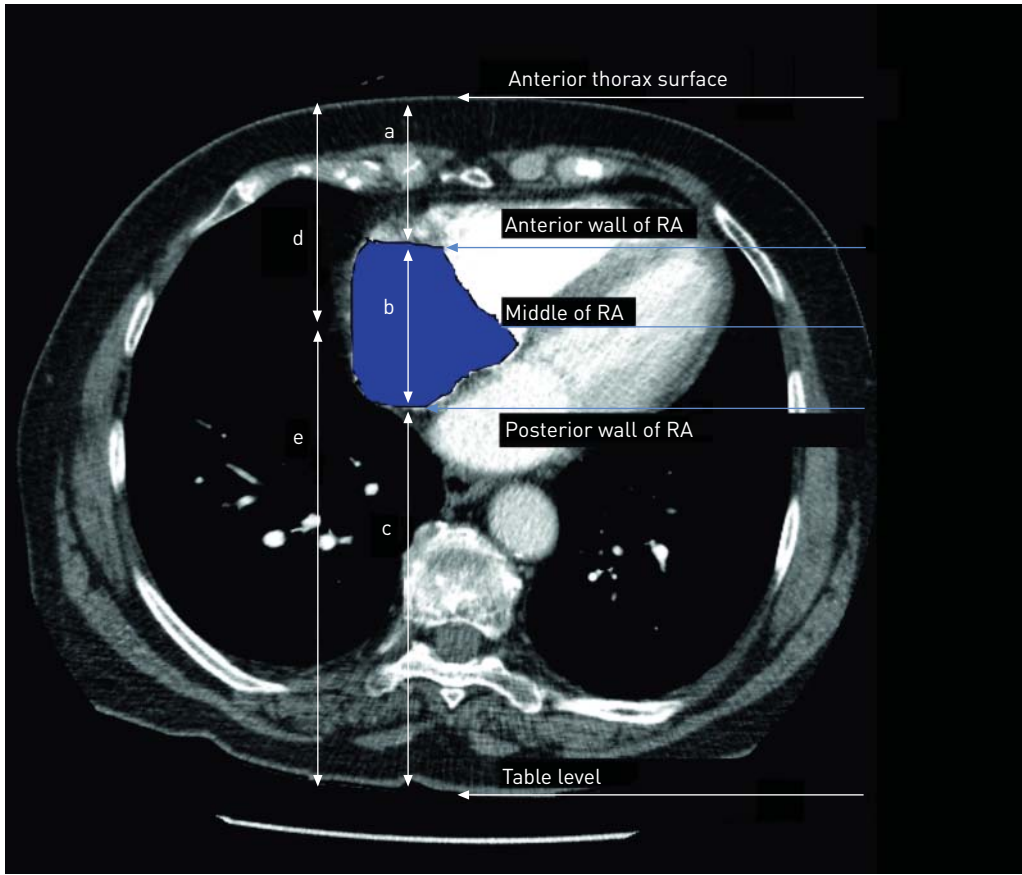


FIGURE 1 Representative computed tomography image showing a) the distance between the anterior skin above sternum and the anterior wall of the right atrium (RA), b) the atrial diameter, c) the distance between the posterior wall of the right atrium and the table level, d) the distance between the anterior skin and the centre of the right atrium and e) the distance between the right atrial centre and the table level.

patients as compared to patients without PH; other intrathoracic measures did not differ significantly among the groups. The thoracic diameter was correlated with body mass index (BMI) ($p < 0.001$, $r = 0.69$), but showed no significant correlation with age ($p = 0.095$, $r = 0.12$) or forced expiratory volume in 1 s ($p = 0.188$, $r = -0.10$).

Out of the four ZRLs analysed, the one at “1/3 thoracic diameter below anterior thorax surface” was localised in 98.5% of patients between the anterior and posterior wall of the right atrium while the ZRL at “10 cm above table level” was only in 3.6% of cases at this level (table 3, fig. 2). The deviation of the analysed four ZRLs from the centre of the right atrium and the pressure differences employing these ZRLs as compared to the centre of the right atrium are represented in table 3 and in supplementary figure S1. Accordingly, the ZRL shift from the mid-atrial level to an alternative ZRL would have changed the classification of PH in 9% (“5 cm below the anterior thorax surface”), 0% (“1/3 thoracic diameter below anterior thorax surface”), 8% (“mid-thoracic level”) and 12% (“10 cm above table level”) of patients (table 4). In addition, such a shift would have led to a relevant change in the PAWP classification (below or above 15 mmHg) in 5%, 2%, 10% and 26% of patients, respectively (table 4).

Regarding the left atrium, the best approximation was reached by the mid-thoracic level (tables 4 and 5, fig. 3), revealing a pressure difference of only 0.2 (-2.0–1.3) mmHg as compared to the left atrial centre level.

When the four analysed ZRLs were compared to one another, the median differences ranged between 2.1 and 8.0 mmHg (table 6). In an obese patient, this difference was as much as 15.4 mmHg. Due to these differences, the switch from ZRL “5 cm below the anterior thorax surface” to ZRL “10 cm above table level” would have led to a change in PH diagnosis in 21% of cases, and to a change in the PAWP class in 31% of cases (table 4).

TABLE 1 Clinical characteristics of patients

	All patients	PH patients	Non-PH patients	p-value
Females/males n/n	114/82	74/61	40/21	0.157
Age yrs	63±14	64±14	59±13	0.001
Height cm	167±9	167±9	167±8	0.824
Weight kg	76±17	76±18	74±15	0.524
Body mass index kg·m ⁻²	27.0±5.8	27.1±6.0	26.6±5.3	0.667
Body surface area m ²	1.8±0.2	1.8±0.2	1.8±0.2	0.671
Mean pulmonary arterial pressure mmHg	33±15	41±12	17±4	
Pulmonary artery wedge pressure mmHg	9±5	10±6	7±3	< 0.001
Pulmonary vascular resistance dyn·s·cm ⁻⁵	437±322	560±316	165±72	< 0.001
FEV ₁ % pred	71±23	68±23	79±19	0.001
FEV ₁ /FVC %	75±12	73±13	77±11	0.029

Data are presented as mean ± SD, unless otherwise stated. PH: pulmonary hypertension; FEV₁: forced expiratory volume in 1 s; FVC: forced vital capacity. Bold indicates statistical significance.

Discussion

In this retrospective study we analysed four different commonly used ZRLs in patients with PH in the supine position. We found that there were relevant differences among these methods, leading to clinically significant differences in the readings of intrathoracic blood pressures. According to our study, the ZRL set to 1/3 of the thoracic diameter below the anterior thorax surface (below the skin above the sternum) would favourably correspond to a ZRL within the right atrium in most patients, while the other commonly used ZRLs would cause significant differences from this reference level. The centre of the left atrium was best described by the “mid-thoracic level”, providing an easily reproducible ZRL, which may be particularly relevant for the assessment of PAWP. According to the normal axial location of the right and left atrium, the insertion of the fourth or fifth rib anteriorly to the body of sternum would be an appropriate axial level for the setting of ZRL in the supine position.

Where is the ideal ZRL?

Every pressure reading during a catheter investigation is a difference between the pressure at the chosen ZRL and in the “chamber or vessel” where the fluid-filled catheter tip is located, provided there is no obstruction and no significant flow within the catheter. According to one classical physiological theory going back to the

TABLE 2 Intrathoracic measures of patients

	All patients	PH patients	Non-PH patients	p-value
RA measurements cm				
Thoracic diameter	25.5±3.5	25.8±3.5	24.9±3.5	0.119
Anterior thorax surface to RA anterior wall	6.0±1.8	5.8±1.8	6.3±1.6	0.111
RA diameter	6.0±1.4	6.6±1.3	4.8±0.9	< 0.001
RA posterior wall to table level	13.5±2.1	13.4±2.1	13.9±2.0	0.133
Anterior thorax surface to mid-RA	9.0±1.7	9.1±1.7	8.7±1.7	0.065
Mid-RA to table level	16.5±2.2	16.6±2.2	16.2±2.2	0.231
Anterior thorax surface to mid-RA:thoracic diameter	0.35±0.03	0.35±0.03	0.35±0.03	0.223
LA measurements cm				
Thoracic diameter	25.2±3.5	25.4±3.5	24.8±3.6	0.221
Anterior thorax surface to LA anterior wall	10.6±1.9	10.7±1.9	10.3±1.8	0.154
LA diameter	3.7±0.9	3.8±0.9	3.5±0.9	0.065
LA posterior wall to table level	10.9±1.7	10.9±1.7	10.9±1.6	0.991
Anterior thorax surface to mid-LA	12.5±2.0	12.6±2.0	12.1±2.1	0.086
Mid-LA to table level	12.7±1.7	12.8±1.7	12.6±1.8	0.638
Anterior thorax surface to mid-LA:thoracic diameter	0.49±0.03	0.50±0.03	0.49±0.02	0.038

Measures derived from thoracic computed tomography scan, as outlined in figure 1. PH: pulmonary hypertension; RA: right atrium; LA: left atrium. Bold indicates statistical significance.

TABLE 3 Distance and calculated pressure differences of zero reference levels (ZRLs) from the centre of the right atrium (RA) and the frequency of ZRLs being at the level of the RA

	Distance from mid-RA level cm	Pressure difference compared to mid-RA level mmHg	Patients with ZRL at the level of the RA
5 cm below anterior thorax surface	-3.9 [-10.3- -0.5]	-3.0 [-8.0- -0.4]	57/196 (29.1%)
1/3 thoracic diameter	-0.4 [-3.8-1.7]	-0.3 [-3.0-1.3]	193/196 (98.5%)
Mid-thoracic level	3.8 [1.7-6.3]	3.0 [1.3-4.9]	49/196 (25.0%)
10 cm above table level	6.5 [1.0-12.1]	5.0 [0.7-9.4]	7/196 (3.6%)

Data are presented as median (range), unless otherwise stated.

end of the 19th century [11], the ZRL should be set at the level of the “physiologic zero point” or “hydrostatic indifferent point” which represents the location in the cardiovascular system where the central venous pressure is tightly regulated, changing little if at all during the volume shifts caused by changes in the position [12, 13]. This point may be found at the junction of “phlebostatic levels” [14] and was supposed to be within the right atrium or in the right ventricle next to the tricuspid valve, but in any case at the level of the right atrium in the supine patient. Accordingly, it has been widely accepted that in the case of PAP and venous pressure measurements, the ideal ZRL should be set at the level of the right atrium [6, 9, 15–17]. However, in the search for the optimal ZRL, it may also be adequate to refer to the level of the left atrium [18, 19], particularly if the diastolic function of the left ventricle is to be analysed.

How to define the level of the right atrium?

There were several efforts to define well recognisable external points which may help to set the ZRL at the level of the right atrium in the supine position. However, there is considerable heterogeneity among the methods, which may be classified into the following approaches: 1) fixed distance from the anterior surface of the chest; 2) fixed distance from the table level; 3) a measure relative to the antero-posterior diameter of the chest; and 4) individual determination by echocardiography or other imaging technique.

The first method was suggested by MORITZ and VON TABORA [6] on the basis of cadaver examinations, and has the advantage of being easy to perform, well reproducible and insensitive to softer underlayment. According to most studies, the ZRL was set at 5 cm below the surface of the thorax. The method was mainly criticised because in individuals with large thoracic diameters this ZRL may be too high, resulting in too low pressure readings [9].

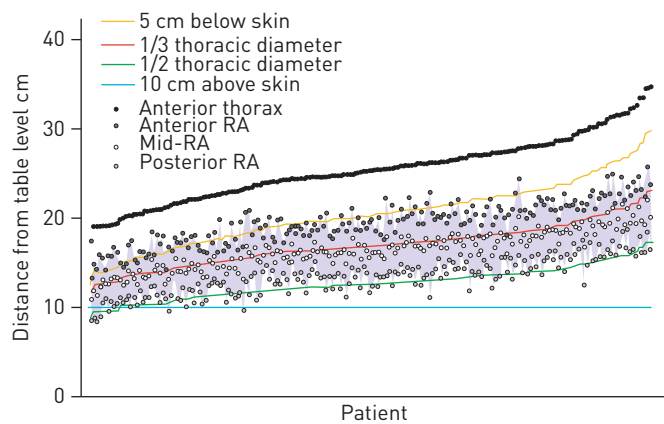


FIGURE 2 Distance of the right atrium from table level. All 196 patients were sorted on the x-axis according to their thoracic diameter in the computed tomography slice optimised for the right atrium (RA). The anterior and posterior walls of the right atrium and the right atrial centre of each patient are given. The blue area represents the distance between the anterior and posterior right atrial wall. Coloured lines represent different zero reference level (ZRL) definitions. It can be seen that the ZRL at 1/3 thoracic diameter is near to the centre of the right atrium in most patients, whereas the ZRL at 5 cm below thoracic surface is around the anterior wall of the right atrium, the ZRL at the mid-thoracic line is mainly around the posterior wall of the right atrium. The ZRL at 10 cm above table level is in most cases below the level of both.

TABLE 4 Percentage of patients (n=196) with mean pulmonary arterial pressure (mPAP) ≥ 25 mmHg versus < 25 mmHg and with pulmonary arterial wedge pressure (PAWP) > 15 mmHg versus ≤ 15 mmHg depending on the chosen zero reference level

	mPAP ≥ 25 mmHg %	mPAP < 25 mmHg %	PAWP > 15 mmHg %	PAWP ≤ 15 mmHg %
5 cm below anterior thorax surface	59	41	7	93
1/3 thoracic diameter	68	32	10	90
Mid-thoracic level	76	24	22	78
10 cm above table level	80	20	38	62
Mid-right atrial level	68	32	12	88
Mid-left atrial level	73	27	22	78

According to the second approach, the ZRL is mostly set at 10 cm from the table level. This approach was also based on cadaver examinations and suggested by LYONS *et al.* [9]. Based on their measurements, normal subjects had the smallest variability by using this approach. The method is widely accepted, easy to perform, but has also been criticised by several authors [10, 20] and comparison studies. The main argument against this method was that in patients with large thoracic diameters the ZRL may be below the level of the heart.

The third approach provides a measure relative to the antero-posterior diameter of the chest. Several options have been suggested, but most frequently the mid-chest level [8, 18], the 1/3 to 2/3 ratio of the thoracic diameter [7, 21, 22], the mid-axillary line [23–25] and the anterior axillary line [26, 27] were used. Comparison studies found these approaches to provide more accurate ZRLs as compared to fixed distances from the anterior thorax surface or the spine [10]. One disadvantage is that the determination of the ZRL is more difficult and may lead to errors and considerable variability, when the method is applied by different and/or inexperienced personal [28].

A fourth method was suggested by COURTOIS *et al.* [29], based upon individual determination of the ZRL by echocardiography. Although the use of the ultrasound approach may appear complex for everyday routine, it might enhance diagnostic accuracy in centres that use the readings for scientific reasons.

In this retrospective study, we used CT images in order to define the true level of the right atrium. This allowed for an unequivocal determination of the centre of the right and left atrium in every single patient. We consider both as possible reference ZRLs. ZRL methods that employed the antero-posterior thoracic diameter appeared to be more accurate as compared to ZRLs with a fixed distance from either the anterior body surface or the table level. The best agreement with the right atrium was found, both in patients with and without PH, when the ZRL “1/3 thoracic diameter below anterior thorax surface” was used, while the ZRL at 10 cm above table level quite poorly predicted the right atrial level. This may be due to the fact that we generally found larger thoracic diameters in our patients compared to most historic cohorts. As thoracic diameter was correlated with BMI, this may be explained by the increase of BMI in the population during the past decades. It may be mentioned that, in the REVEAL registry, the BMI of PH patients was even higher than in our cohort [30]; therefore, the impact of ZRL definition would have even been larger than in our study. For the left atrial level, the mid-thoracic line was most adequate in nearly all our patients. This suggests that, for scientific questions related to left ventricular function, the ZRL at the mid-thoracic level might be ideal.

TABLE 5 Distance and calculated pressure differences of zero reference levels (ZRLs) from the centre of the left atrium (LA) and the frequency of ZRLs being at the level of the LA

	Distance from mid-LA level cm	Pressure difference compared to mid-LA level mmHg	Patients with ZRL at the level of the LA
5 cm below anterior thorax surface	-7.4 [-14.6– -3.3]	-5.8 [-11.4– -2.6]	0/196 [0%]
1/3 thoracic diameter	-4.1 [-8.2– -2.0]	-3.2 [-6.4– -1.6]	0/196 [0%]
Mid-thoracic level	0.2 [-2.5–1.7]	0.2 [-2.0–1.3]	191/196 [97.4%]
10 cm above table level	2.7 [-1.5–7.0]	2.1 [-1.2–5.5]	61/196 [31.1%]

Data are presented as median (range), unless otherwise stated.

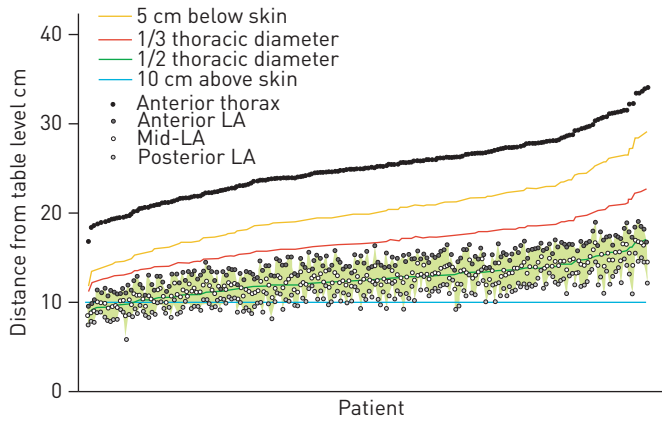


FIGURE 3 Distance of the left atrium from table level. All 196 patients were sorted on the x-axis according to their thoracic diameter in the computed tomography slice optimised for the left atrium (LA). The anterior and posterior walls of the left atrium and the left atrial centre of each patient are given. The green area represents the distance between the anterior and posterior left atrial wall. Coloured lines represent different zero reference level definitions. It can be seen that the mid-thoracic level hits the left atrium in most patients.

Clinical relevance

How do differences between ZRLs lead to pressure differences? As the specific gravities for blood and mercury are 1.055 and 13.6, a blood column of 1 cm is equivalent to a mercury column of 0.78 mm. Accordingly, by shifting the ZRL from the mid-atrial ZRL to “5 cm below anterior thorax surface”, the percentage of patients in our patient cohort with mean PAP ≥ 25 mmHg would decrease from 68% to 59%, while shifting the ZRL to the level “10 cm above table level” would increase this percentage to 80% (table 4). Similar changes may be observed regarding PAWP. PAWP readings are of special relevance for the diagnosis of pulmonary arterial hypertension, because readings >15 mmHg preclude this diagnosis [1]. Notably, in their description of left atrial pressures in normal subjects, BRAUNWALD and co-workers set the ZRL at 5 cm below the anterior thorax surface and found that the normal left atrial pressure never exceeded 12 mmHg [31, 32]. However, other ZRLs, such as 10 cm above table level, would have resulted in significantly higher values [33]. Therefore, one of the major confounding factors for any definition of the “normal range of PAWP” is the definition of ZRL. This may be of special interest when the upper limit of PAWP is considered among the inclusion criteria of PAH studies, as the 15 mmHg cut-off value using the 1/3-thoracic diameter ZRL would be very close to the 12 mmHg cut-off level described by BRAUNWALD *et al.* [31] using the ZRL 5 cm below the sternal angle.

Unfortunately, in different countries, different cities, and even within centres, different ZRL methods have been used and there is no consensus on a gold standard. This may lead to therapeutic consequences for patients, particularly in the obese population. Therefore, a uniform definition of ZRL should be established, in order to avoid discrepancies and misconceptions about the definitions of PH and elevated left heart pressures. Remarkably, independent of BMI and thoracic diameter, the reference line at 1/3 thoracic diameter remained representative for the right atrium and the one at 1/2 thoracic diameter for the left atrium in our study. When choosing the appropriate ZRL, besides physiological considerations, also the practicability and reproducibility of the method has to be taken into account [28]. This might speak in favour of the mid-thoracic level.

Limitations

In this manuscript, we focused on the influence of ZRL on pressure readings in the supine position. We did not address other important issues such as the role of in- and expiration [34], intrathoracic pressure and its changes caused by obstructive or restrictive lung diseases and by exercise. In addition, we did not address the question, where the ZRL should be placed in the upright or semi-upright positions. Based on the “phlebostatic axis” theory, in the sitting position, the use of the fourth intercostal space for ZRL may be the

TABLE 6 Pressure differences between zero reference levels

	5 cm below anterior thorax surface	1/3 thoracic diameter	Midthoracic level
1/3 thoracic diameter	2.7 [0.6–5.1]		
midthoracic level	6.0 [2.9–9.6]	3.3 [2.3–4.5]	
10 cm above table level	8.0 [2.0–15.4]	5.4 [1.3–10.2]	2.1 [–1.0–5.7]

Data are presented as median (range).

most widespread one [14]. We feel that all these mentioned factors are very important for the interpretation of pressure readings, but they cannot be addressed adequately, if there is no consensus on the ZRL in the supine position.

Our chest CT readings may have included the vena cava confluens as part of the right atrium in some patients, leading to a slight overestimation of right atrial diameters. This may have influenced the localisation of the posterior wall of the right atrium, causing a minor error in the determination of the centre of the right atrium.

The choice of the CT slice for the thoracic diameter measurement was based on the optimal presentation of the right or left atrium in the chest CT, and not on an anatomical landmark. The detected diameters showed only minimal differences (0.3 ± 0.5 cm) between these two slices. Therefore, in the absence of major thoracic deformities, a significant effect of these differences appears unlikely.

The proportion of patients with changes in final diagnosis due to the change of ZRL is dependent on the examined population. This rate may have been different in a centre, where more patients with congestive heart failure or less patients with slightly elevated PAP values would have been investigated than in our study. This, however, does not question the necessity of standardisation.

Conclusion

The four most commonly used methods for ZRL setting result in significantly different thoracic blood pressure readings and may significantly influence the classification of PH patients. As long as there is no international standard, the method of zeroing should be provided in each study on haemodynamics.

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