

1 **Significance of internal auditory canal diverticula in ears with otosclerosis**

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14 Running title: internal auditory canal diverticulum

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1 **Abstract**

2 Background: Diverticula in the internal auditory canal (IAC) have been reported in  
3 ears with otosclerosis. Objective: We evaluated hearing levels and vascular activity in  
4 ears with otosclerosis with and without IAC diverticula and clarify the significance of  
5 IAC diverticula. Materials and Methods: Sixty-one ears from 54 patients who  
6 underwent stapes surgery for otosclerosis (fenestral (48 ears) and retrofenestral (13  
7 ears) groups) were included in the present study. Preoperative hearing levels on pure  
8 tone audiometry (PTA) and intraoperative measurements of blood flow were  
9 compared between the groups. Results: A total of 24 of 61 ears (39.3%) showed IAC  
10 diverticula, significantly higher than the frequency in ears without otosclerosis (3.7%).  
11 No significant differences in air- and bone-conduction thresholds on PTA were  
12 evident between ears with and without IAC diverticula in each group. Ears without  
13 IAC diverticula tended to show higher blood flow in the area anterior to the oval  
14 window than ears with IAC diverticula, but the difference was not significant.  
15 Conclusions: The incidence of the IAC diverticula in otosclerosis was significantly  
16 higher than in cases without otosclerosis. The existence of IAC diverticula was not  
17 evidently related to the severity of the disease from the perspective of hearing level  
18 and vascular activity.

19

20 **Key words:** internal auditory canal diverticulum, otosclerosis, hearing level, blood  
21 flow, laser-Doppler flowmetry

1 **1. Introduction**

2 Otosclerosis is a progressive osteodystrophy disease of the otic capsule and is  
3 characterized by bony resorption, vascular proliferation, and sclerotic new bone  
4 formation [1]. Otosclerosis is categorized into two types: fenestral type, which shows  
5 overgrowth of hypoattenuating bone in the region of the fissula ante fenestram; and  
6 retrofenestral type, which shows a hypoattenuating halo around the cochlea. The  
7 retrofenestral type usually occurs with fenestral involvement, and these manifestations  
8 are considered to be on a continuum rather than two separate entities [2].

9 The existence of an internal auditory canal (IAC) diverticulum, which is detected as a  
10 small focal outpouching arising from the anterolateral wall of the IAC on computed  
11 tomography (CT), has been reported in ears with otosclerosis. Such diverticula are  
12 considered cavitory lesions of otosclerosis [3,4]. The pathophysiology of the IAC  
13 diverticula is not clear, and the prevalence may be related to the severity of  
14 otosclerosis [5]. A recent study reported that the lesions were associated with  
15 sensorineural hearing loss (SNHL), regardless of the concomitant existence of  
16 otosclerosis [6].

17 Vascularity appears to be a factor in the pathology of otosclerosis, and active and  
18 inactive otospongiotic or otosclerotic lesions in ears with otosclerosis can be  
19 histologically classified by different types of vascularity [7]. A pathologic feature of  
20 otosclerosis is new vessel formation, which is most pronounced when the disease is  
21 active [7,8]. Active otosclerosis could accompany increased vascularity, and  
22 intraoperative measurement of blood flow using laser Doppler flowmetry has been  
23 reported to yield useful information about the progress of vascular activity in ears  
24 with otosclerosis [9].

1 This study aimed to compare hearing levels and vascular activity in ears with  
2 otosclerosis with and without IAC diverticula and to clarify the association between  
3 the existence of IAC diverticula and the severity of the disease.

4

5 **2. Patients and methods**

6 Sixty-one ears from 54 patients (21 males, 33 females; age range, 31-72 years) who  
7 underwent stapes surgery for otosclerosis in our hospital were included in the present  
8 study. All patients underwent preoperative pure-tone audiometry (PTA) and CT using  
9 sequential 0.5-mm-thick slices. The surgical findings confirmed the final diagnosis of  
10 otosclerosis in all ears.

11

12 **2.1. Hearing levels on PTA**

13 Air-conduction (AC) and bone-conduction (BC) thresholds were determined at 0.5, 1,  
14 2, and 4 kHz on PTA (AA-78; Rion, Tokyo, Japan), and mean hearing threshold at  
15 these frequencies was calculated in each ear.

16

17 **2.2. Evaluation on CT**

18 Based on CT (Asteion and Aquilion; Toshiba, Tokyo, Japan) imaging findings, ears  
19 were preoperatively classified into the following two types of otosclerosis: i) subjects  
20 with hypoattenuating lesions limited to areas anterior to the oval window (OW)  
21 (fenestral group); and ii) subjects with hypoattenuating lesions that extended over the  
22 labyrinth capsules (retrofenestral group) [9]. IAC diverticulum was defined as an  
23 obvious notch and low attenuation in the anterior IAC margin. Foci varied in size  
24 from a small focal notch to a larger diverticulum, and a diverticulum was considered

1 present when the depth was larger than 0.5 mm. Example images from ears with and  
2 without an IAC diverticulum are shown in Figure 1.

3 As a control, investigation of IAC diverticula was also applied on ears without  
4 otosclerosis, which had neither hypoattenuating lesions suggesting otosclerosis nor  
5 anomaly of the inner ear on CT. The group comprised 81 patients (27 males, 54  
6 females; age range, 9-81 years), and all underwent ear surgeries for the following  
7 disease: acquired profound sensorineural hearing loss, 44 cases; ossicular anomalies,  
8 18 cases; perilymphatic fistula, 7 cases; external auditory canal disease, 5 cases; facial  
9 palsy, 4 cases; and traumatic interruption of ossicular chain, 3 cases.

10

11 **2.3 Measurement of blood flow**

12 Measurements of blood flow were performed with a laser Doppler flowmeter (LDF,  
13 model ALF 21, Advance, Tokyo, Japan), as described elsewhere [9]. Briefly, the tip of  
14 the probe was attached manually to two portions: the anterior portion of the OW  
15 directed to the fissula ante fenestram (defined as the blood flow in the AOW); or the  
16 promontory (PT) located 1.5 mm inferior to the OW (defined as the blood flow in the  
17 PT). After the blood flow had stabilized, 5-s mean values were obtained. No  
18 additional procedures, such as removal of the mucosa in the region, were performed  
19 during measurement.

20 Statistical analyses were conducted using the independent-samples *t*-test and  
21 Mann-Whitney U test with SPSS 25.0. Values of  $P < 0.05$  were considered significant.  
22 Written, informed consent was obtained preoperatively from each patient, and the  
23 study protocol was approved by the institutional review board at Nagoya University  
24 Hospital.

25

1 **3. Results**

2 Based on CT images, 48 ears were enrolled in the fenestral group and 13 ears were  
3 enrolled in the retrofenestral group. A total of 24 of 61 ears (39.3%) had IAC  
4 diverticula, which included 17 ears (35.4%) in the fenestral group and 7 ears (53.8%)  
5 in the retrofenestral group. Fifteen of 19 (78.9%) patients had bilateral IAC  
6 diverticula, including 9 of 13 patients (69.2%) and 6 of 6 patients (100%) in the  
7 fenestral and retrofenestral groups, respectively, although only five patients  
8 underwent surgery of both ears. As for the control group, 6 ears (4 cases) of the 162  
9 ears (81 cases) had IAC diverticula (3.7%), and their diagnosis was profound  
10 sensorineural hearing loss in 3 ears (2 cases), facial palsy in 2 ears (1 case), and  
11 traumatic interruption of the ossicular chain in 1 ear (1 case). The incidence of IAC  
12 diverticula in otosclerosis was significantly higher in both the fenestral and  
13 retrofenestral group than in the control group.

14 Table 1 shows the average AC and BC thresholds at four frequencies and the mean  
15 hearing threshold on PTA in the fenestral group. There was no significant difference  
16 in each hearing threshold between ears with and without IAC diverticula in the group.

17 Table 2 shows the average AC and BC thresholds at four frequencies and the mean  
18 hearing threshold on PTA in the retrofenestral group. No significant difference in each  
19 hearing threshold was evident between ears with or without IAC diverticula in each  
20 group.

21 Figure 2 shows the values of blood flow in the AOW and PT in the fenestral group.  
22 Some ears without an IAC diverticulum showed relatively higher blood flow values in  
23 the AOW than those with a diverticulum, but the average arbitrary units (AU:  
24 mL/min/100 g) in ears without and with IAC diverticula were 5.4 and 3.8,  
25 respectively, showing no significant difference (p=0.48). Meanwhile, values of blood

1 flow in the PT were similar between groups: average AUs in ears without and with  
2 IAC diverticula were 4.2 and 4.7, respectively.  
3 Figure 3 shows the values of blood flow in the AOW and PT in the retrofenestral  
4 group. Some ears without an IAC diverticulum showed relatively higher blood flow  
5 values in the AOW than those with a diverticulum, but averages in ears without and  
6 with IAC diverticula were 7.3 and 2.6 AU, respectively, showing no significant  
7 difference ( $p=0.095$ ). Average values of blood flow in the PT of ears without and with  
8 IAC diverticula were 11.7 and 10.3 AU, respectively, and values were similar between  
9 groups.

10

#### 11 **4. Discussion**

12 Etiological factors of otosclerosis have yet to be elucidated, but include autoimmunity,  
13 genetics, inflammation, viruses, and hormonal influences [10]. The most common site  
14 of the lesion is the fissula ante fenestram, followed by the round window niche, apical  
15 and medial cochlear walls, and anterior wall of the IAC [11,12].

16 The presence of IAC diverticula has been reported in limited cases, and the  
17 pathophysiology remains unclear. An IAC diverticulum might reflect a cavitory lesion  
18 of otosclerosis and represent a variant of cochlear otosclerosis [3,4], which could  
19 involve a much more extensive cavitation phenomenon in the otic capsule of patients  
20 with this disease [3]. Another reported assumption is that IAC diverticula are related  
21 to SNHL in a different pattern than the classic CT presentation of otosclerosis [6],  
22 although these lesions occasionally present in otosclerosis. In the present study, the  
23 incidence of an IAC diverticulum in ears with otosclerosis was 39.3%, significantly  
24 higher than in the control group. This finding might suggest a relationship between  
25 otosclerosis and the presence of IAC diverticula to some extent.

1 The retrofenestral type of otosclerosis could cause conductive hearing loss, mixed  
2 hearing loss, or SNHL [13], in which direct injury to the cochlea and spiral ligament  
3 due to the lytic process or release of proteolytic enzymes might cause SNHL [14]. The  
4 present study showed no significant differences in AC and BC thresholds between  
5 ears with and without IAC diverticula, both in the fenestral and retrofenestral group.  
6 This finding does not support IAC diverticulum as a cause of SNHL in ears with  
7 otosclerosis.

8 The early phase of otosclerosis is characterized by the presence of spongy irregular  
9 vascular foci of demineralized bone with osteoplastic bone resorption. These foci then  
10 become less vascular and tend to calcify, forming dense bone. Active resorption and  
11 bone deposition are often present in the same focus of otosclerosis [15,16]. The  
12 vascular activity may reflect the lesion process, which could be evaluated by  
13 intraoperative laser Doppler flowmetry [9]. The present study showed no significant  
14 differences in values of blood flow in the AOW and PT between ears with and without  
15 IAC diverticula in both the fenestral and retrofenestral group. Some ears without an  
16 IAC diverticulum in both groups showed relatively higher values of blood flow in the  
17 AOW, where the most common site of the lesion is the fissula ante fenestram. At this  
18 point, ears with IAC diverticula may not have a more active vascular process than  
19 those without IAC diverticula, though interpretation of this finding is difficult.

20 Several limitations to the present study must be considered, including the small  
21 sample size and the methods of evaluation. Other aspects besides hearing thresholds  
22 or blood flow should be considered to evaluate otosclerosis activity concerning the  
23 significance of IAC diverticula in ears with the disease. We are planning future  
24 studies to further clarify this issue.

25



1 **5. Conclusions**

2 IAC diverticulum was significantly more frequent in otosclerosis in both the fenestral  
3 and retrofenestral group than in the control group, although the rate tended to be  
4 higher in the retrofenestral group. The existence of IAC diverticula did not appear  
5 related to the severity of disease assessed using hearing levels and vascular activity.

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1 **Figure legends**

2 Figure 1: Example images from ears with (A) and without (B) an internal auditory  
3 canal (IAC) diverticulum. An IAC diverticulum can be detected as an obvious notch  
4 in the anterior wall of the IAC (A, arrow).

5

6 Figure 2: Values of blood flow in (A) areas anterior to the oval window and (B) the  
7 promontory of ears with and without an internal auditory canal diverticulum in the  
8 fenestral group. (A.U., arbitrary units)

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10 Figure 3: Values of blood flow in (A) areas anterior to the oval window and (B) the  
11 promontory of ears with and without an internal auditory canal diverticulum in the  
12 retrofenestral group. (A.U., arbitrary units)

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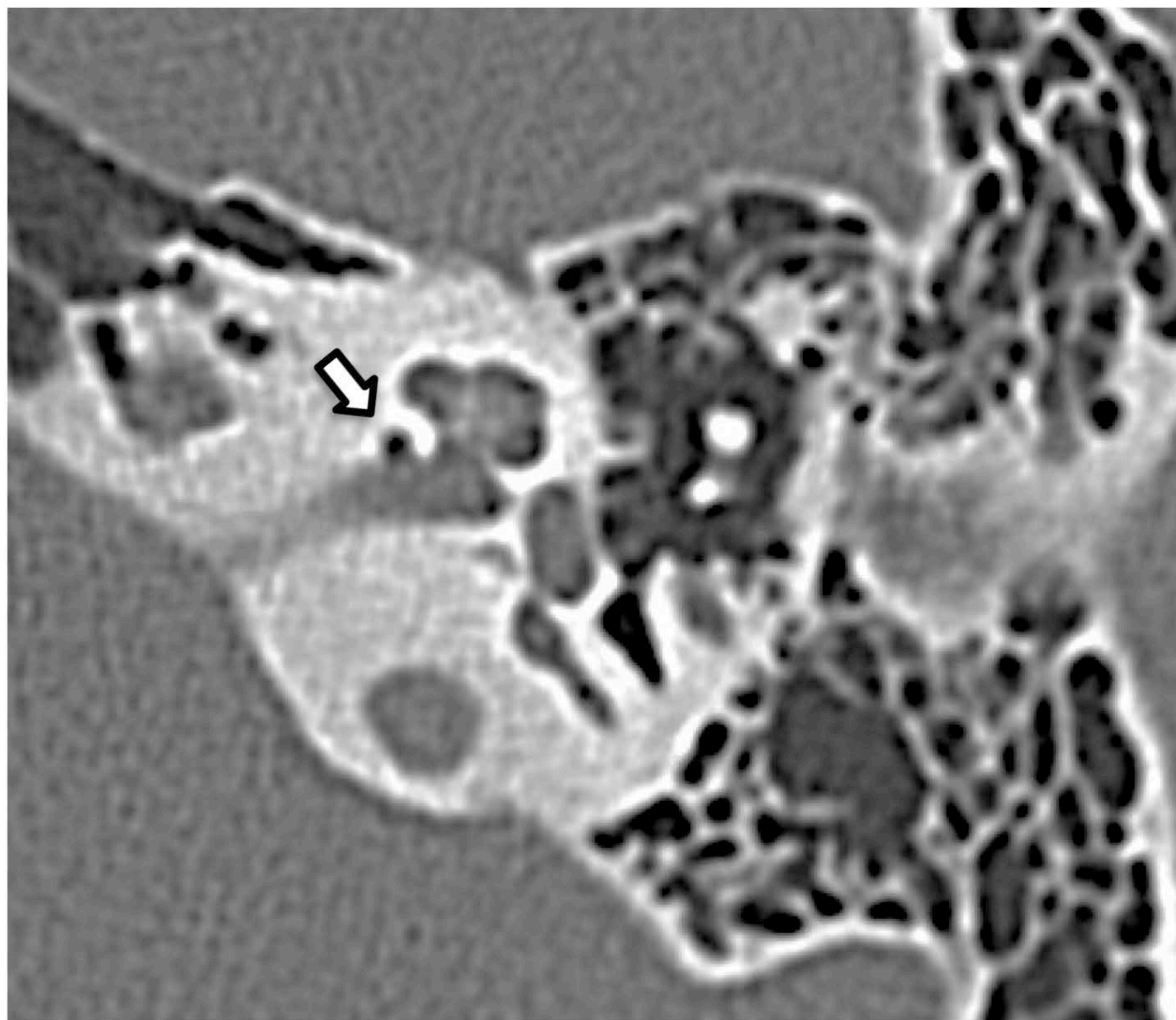
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Table I: Average air- and bone-conduction thresholds (AC and BC) at four frequencies and mean hearing thresholds in ears with and without an internal auditory canal diverticulum in the fenestral group

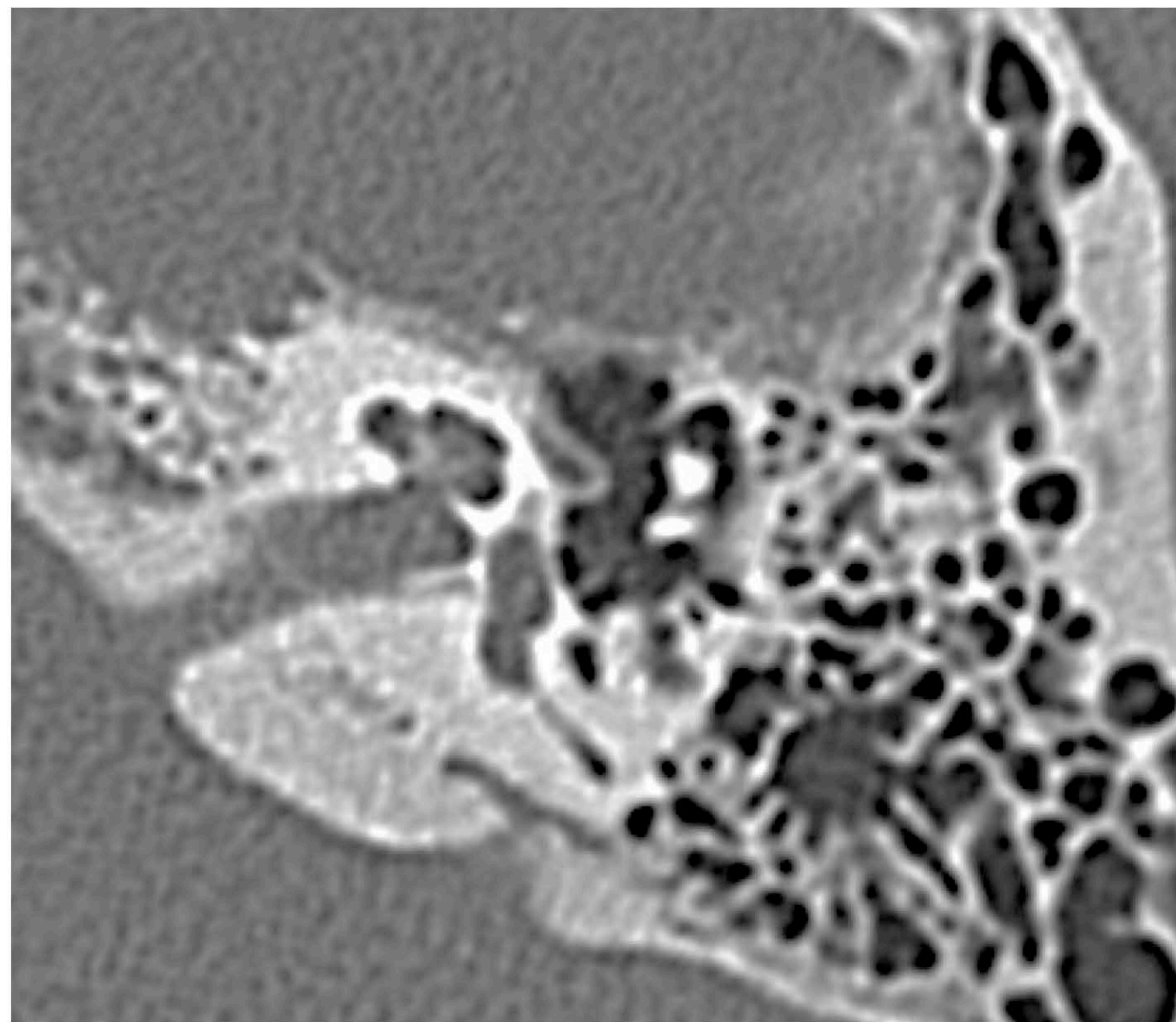
		<b>500 Hz</b>	<b>1000 Hz</b>	<b>2000 Hz</b>	<b>4000 Hz</b>	<b>Mean</b>
<b>With</b>	<b>AC</b>	65.0	62.1	55.8	48.7	57.9
	<b>BC</b>	18.1	29.2	38.2	24.8	27.6
<b>Without</b>	<b>AC</b>	66.4	60.6	55.0	46.2	57.1
	<b>BC</b>	15.6	26.2	32.9	24.1	24.7

Table II: Average air- and bone-conduction thresholds (AC and BC) at four frequencies and mean hearing thresholds in ears with and without an internal auditory canal diverticulum in the retrofenestral group

		<b>500 Hz</b>	<b>1000 Hz</b>	<b>2000 Hz</b>	<b>4000 Hz</b>	<b>Mean</b>
<b>With diverticulum</b>	<b>AC</b>	62.5	60.0	55.0	55.0	58.1
	<b>BC</b>	28.3	29.2	40.0	34.2	32.9
<b>Without diverticulum</b>	<b>AC</b>	67.9	70.0	71.4	74.3	70.9
	<b>BC</b>	28.6	32.9	50.7	43.6	38.9



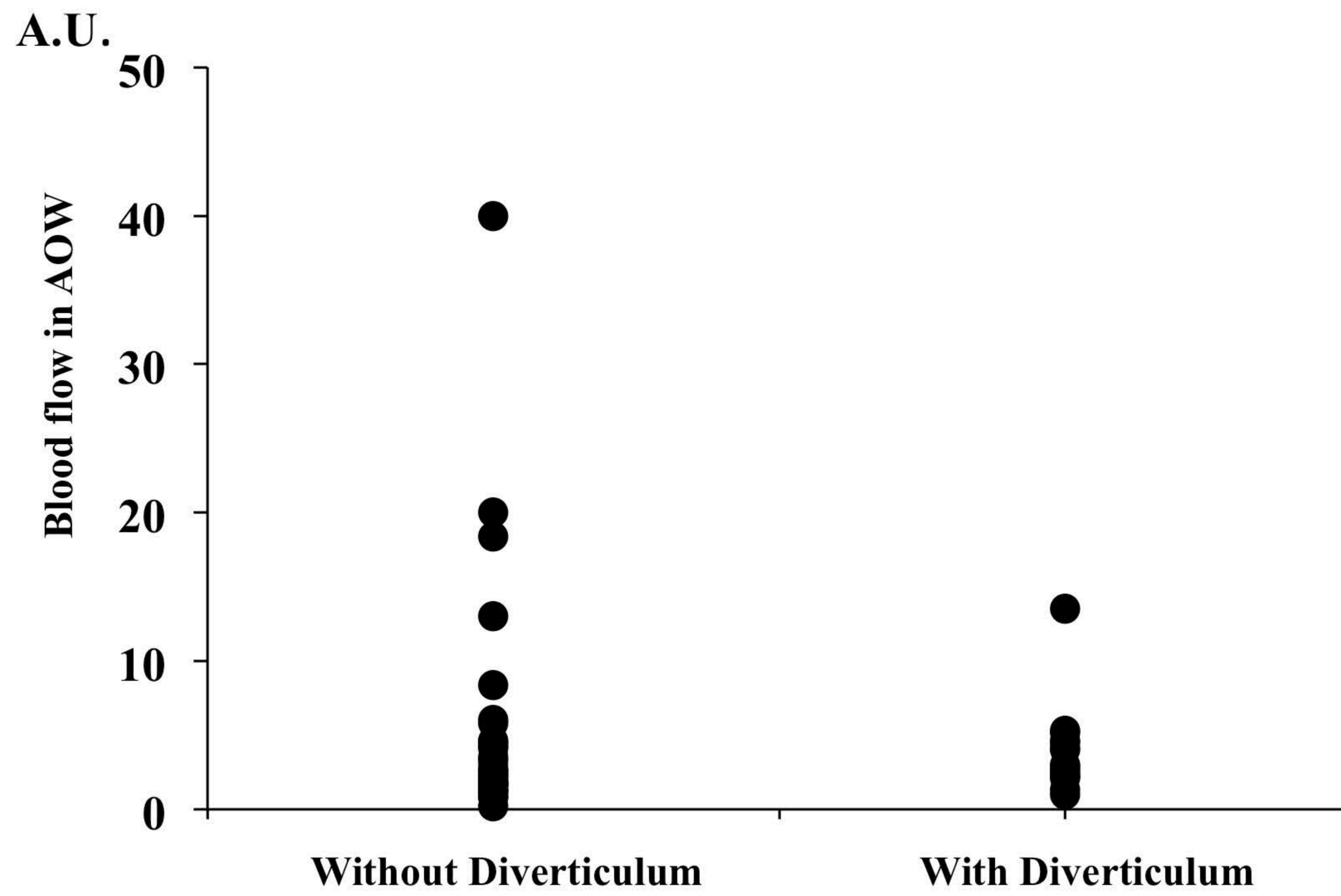
**A)**



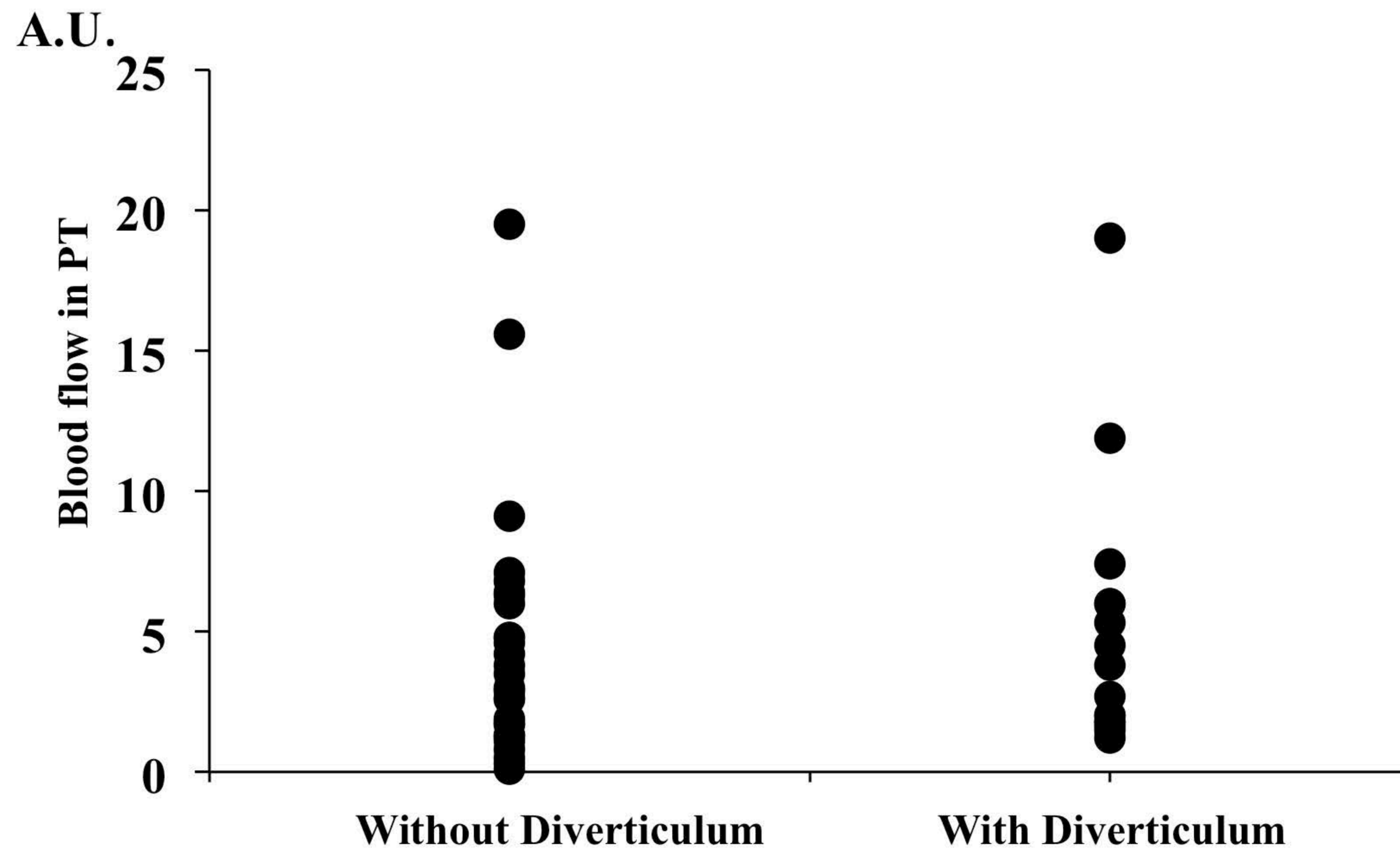
**B)**

**Figure 1**

**A)**



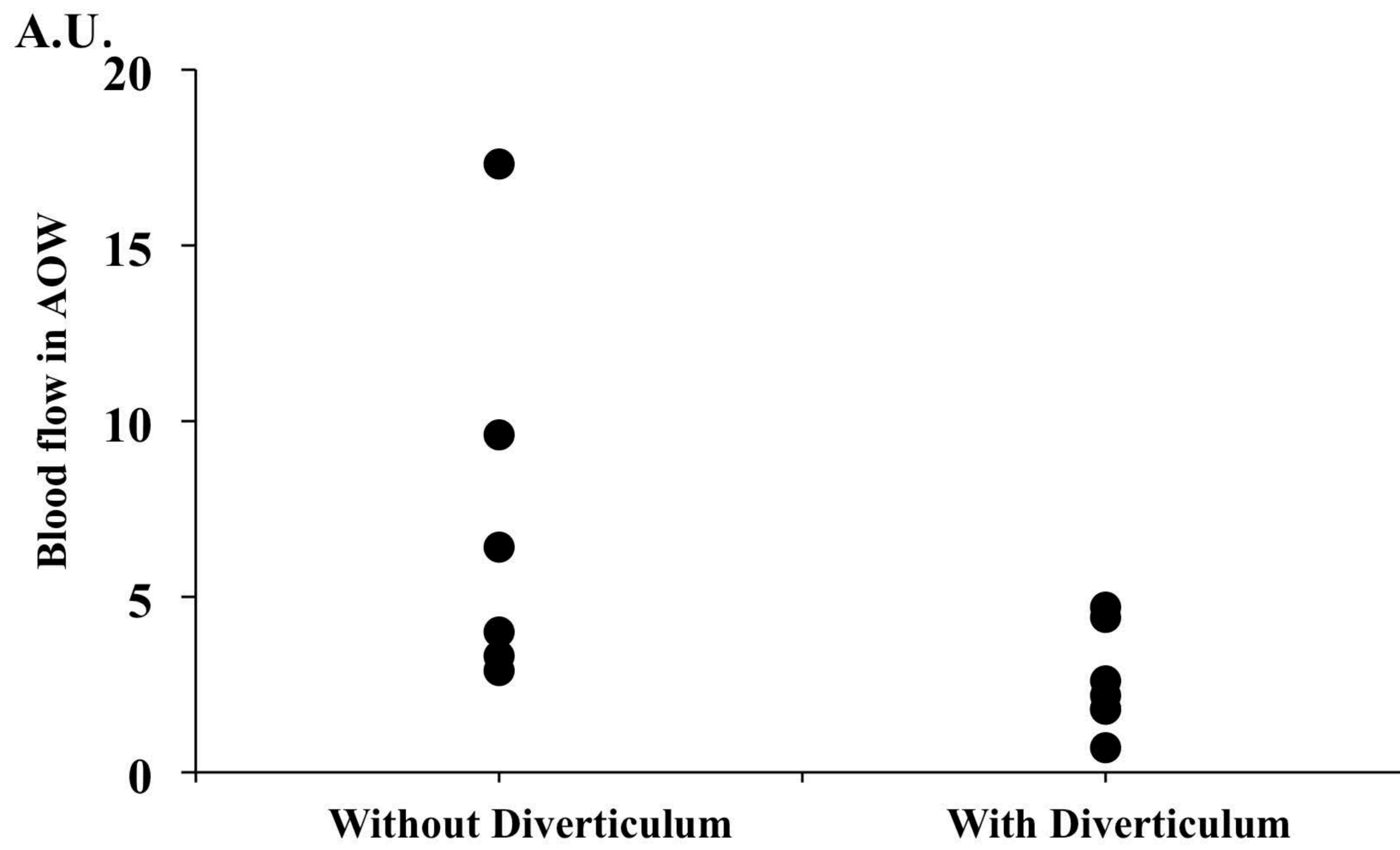
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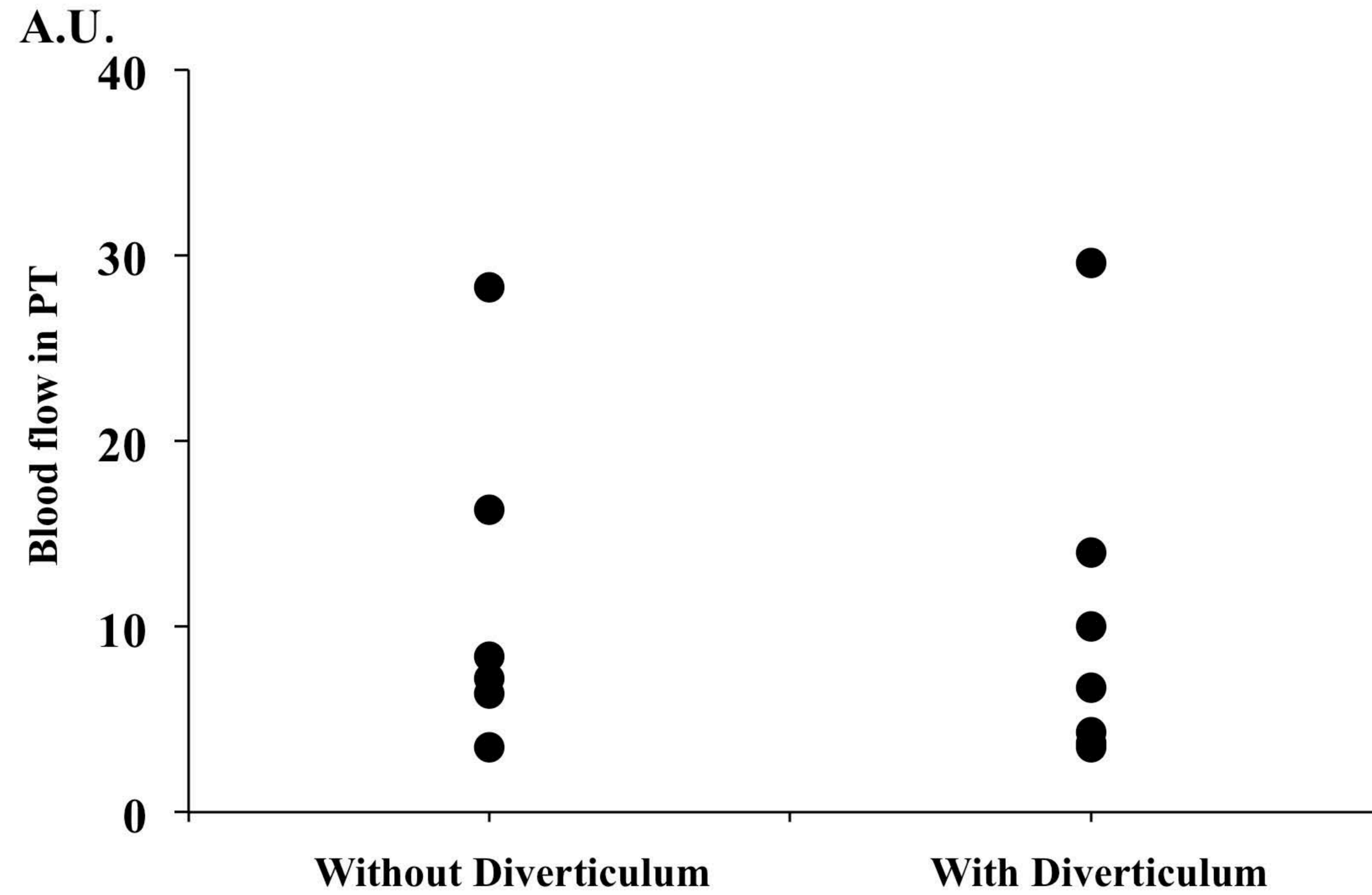
**Figure 2**



**A)**



**B)**



**Figure 3**