Lateralization of renal blood flow and renin secretion in fibromuscular dysplasia Reply

condition of insufficient compensatory BP increase. Although van Twist *et al.* [1] examined RBF and RRS after discontinuation of antihypertensive medication, the examination in RVH needs to be done under suppression of the renin–angiotensin cascade [5].

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Conflicts of interest

There are no conflicts of interest.

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Reply

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We appreciate the interest of Dr Tanemoto [1] in our study on the pathophysiological differences between multifocal fibromuscular dysplasia (FMD) and atherosclerotic renal artery stenosis (ARAS) [2]. Although we agree with Dr Tanemoto that the mechanisms leading to hypertension in multifocal FMD remain to be elucidated, we do not agree with his view that the absence of lateralization in renin secretion in patients with unilateral multifocal FMD is the result of compensatory systemic hypertension that maintains blood flow in the affected kidney.

First of all, if mean renal blood flow (MRBF) in the affected kidney is indeed preserved because of systemic hypertension, it would inevitably lead to hyperperfusion (and thus lateralization in MRBF) and hyperfiltration in the contralateral nonaffected kidney, which is, as we both previously demonstrated [2,3], not the case. Moreover, hyperperfusion would presumably induce reactive vasoconstriction (to normalize MRBF) in the nonaffected kidney, which on its turn would suppress renin secretion in that kidney and thus induce lateralization in renin secretion. Second, if hypertension in multifocal FMD is indeed driven by increased renin secretion, one would have expected that at least a little lateralization in renin secretion was observed in some patients (at least in those in the early stage of renovascular hypertension or those with more severe hemodynamic changes). This, however, was not the case [2,3]. Furthermore, renin secretion in FMD was comparable with that in patients with essential hypertension and the response to intrarenal infusion of angiotensin II and angiotensin-(1–7) revealed no signs of intrarenal renin–angiotensin system overactivity in the affected kidney [3]. Moreover, blockade of the renin–angiotensin system (as suggested by Dr Tanemoto) by infusion of eprosartan increased (instead of decreased) renal blood flow in the affected kidney [3]. Third, the suggested presence of collateral vessels (which is, in our experience, rare in multifocal FMD) would not explain why blood pressure (BP) decreases after balloon angioplasty, as flow was already restored by the collaterals. Fourth, given the differences in dimensions of the vascular lumen between the two-kidney one-clip model and multifocal FMD (external compression on one point vs. intraluminal webs and aneurysms over a longer segment) and thus its hemodynamic effect, we do not believe that it is appropriate to use the two-kidney one-clip model as a model for renovascular hypertension due to multifocal FMD. Perhaps, it could serve as a model for unifocal FMD [4], but that is still subject to research.

Finally, we demonstrated that lateralization in renin secretion is present in a large subset of patients with unilateral ARAS [2], which would indicate that the suggested compensatory mechanism is not present or insufficient in those patients. This, together with our observations of a preserved MRBF, 'normal' renin secretion, and an inverse relationship between renin levels and BP in patients with multifocal FMD, strongly indicates that the mechanisms leading to renovascular hypertension in multifocal FMD truly differ from those in ARAS. Therefore, future studies (perhaps with new animal models) are needed to elucidate the underlying mechanisms inducing hypertension in patients with multifocal FMD.

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Conflicts of interest

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Antihypertensive medication use and breast cancer risk

Kadri Altundag

I want to congratulate Yang *et al.* [1] for their article in which they evaluated blood pressure and risk of breast cancer in a prospective cohort study. The authors did not find any association between blood pressure and breast cancer. However, the authors did not give information about the association between antihypertensive medication use and breast cancer risk. An interesting study by Largent *et al.* [2] investigated the association between hypertension, antihypertensive medication use, and breast cancer in a large prospective study. They reported that when compared with no use, use of antihypertensive medication for at least 5 years was associated with a modest increased risk of invasive breast cancer. As in the current study almost 14–17% of cases were reported to use antihypertensive medication at baseline, these cases might be analyzed separately for subsequent breast cancer risk.

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The article does not contain any studies with human participants or animals performed by any of the authors.

Conflicts of interest

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Reply

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We thank Altundag [1] for his interest in our recent study [2] and welcome his suggestion to present additional data regarding use of antihypertensive medication and breast cancer risk.

We have summarized in Table 1 the additional analyses we conducted using Cox models, following the same methodology as in our study. We found no evidence that the risk of breast cancer was increased for women taking antihypertensive medication [compared with nonusers: hazard ratio = 0.96, 95% confidence interval (CI): 0.83–1.11, based on 246 cases]. This finding is somewhat different to that of Largent *et al.* [3], who reported an increased risk associated with long-term antihypertensive medication

TABLE 1. Use of antihypertensive medication at baseline and risk of breast cancer overall, and by menopausal and estrogen-receptor status

	n^a		n^a	HR[b]	95% CI	*P*
Overall	1380	Nonusers	1134	Reference		
		Users	246	0.96	0.83, 1.11	0.58
Premenopausal	503	Nonusers	456	Reference		
		Users	47	1.23	0.90, 1.60	0.19
Postmenopausal	877	Nonusers	678	Reference		
		Users	199	0.91	0.78, 1.08	0.29
ER+	1011	Nonusers	823	Reference		
		Users	188	0.97	0.82, 1.15	0.73
ER−	301	Nonusers	258	Reference		
		Users	43	0.84	0.60, 1.18	0.32

HR: hazard ratio, ER+/−: estrogen receptor-positive/negative.
[a]Number of breast cancer cases.
[b]Adjusted for country of birth, waist circumference, physical activity, alcohol consumption, smoking, Mediterranean Diet Score, use of hormonal replacement therapy and oral contraceptive, parity, socioeconomic status, and level of education.