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N-terminal pro-brain natriuretic peptide — a promising biomarker for the diagnosis of left ventricular hypertrophy in hypertensive women

Le peptide natriurétique de type B, fragment terminal (NT-Pro-BNP), un marqueur prometteur pour le diagnostic d'hypertrophie ventriculaire gauche chez les femmes hypertendues

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Summary

Introduction. — No agreement has been reached regarding the best strategy to detect left ventricular hypertrophy (LVH). This study examined the role of N-terminal pro-brain natriuretic peptide (NT-proBNP) in the diagnosis of LVH in hypertensive patients and the potential factors that may influence its diagnostic performance.
Methods. — The global accuracy of NT-proBNP in diagnosing LVH was assessed using a receiver-operating characteristic (ROC) curve. The influence of patients' characteristics on test accuracy was studied with a ROC regression based on a probit model. Ninety-three subjects were

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**Sex factors;
Sensitivity and
specificity**

included. All had NT-proBNP measured and underwent electrocardiography and echocardiography, with calculation of the left ventricular mass index (LVMI).

Results. — The diagnostic performance of NT-proBNP in LVH varied slightly depending on the indexation mode of LVMI. In cases of body surface area indexation, the area under the ROC curve of 81.6% suggested a good performance. The accuracy of the marker was significantly higher in women than in men ($p < 0.0001$). There were no significant effects of age, treatment, body mass index, left ventricular mass index, 24-h systolic blood pressure, or creatinine clearance on the test performance. Slight differences were observed when an indexation to height$^{2.7}$ instead of body surface area was used.

Conclusions. — The present results may lead to a new strategy for risk stratification in hypertension: in women, NT-proBNP alone or preferably in combination with electrocardiography seems sufficient to confirm or exclude diagnosis of LVH. In men, echocardiography would only be needed in cases of negative electrocardiography and NT-proBNP test.

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MOTS CLÉS

Hypertension
artérielle ;
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Facteurs de sexe ;
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Résumé

Introduction. — Il n'y a pas de consensus concernant la meilleure stratégie pour détecter une hypertrophie ventriculaire gauche (HVG). Cette étude a évalué le rôle du NT-pro-BNP (peptide natriurétique de type B, fragment terminal) dans le diagnostic de l'HVG chez les patients hypertendus, ainsi que les facteurs potentiellement associés qui pourraient influencer la performance diagnostique.

Méthode. — La précision globale du NT-pro-BNP dans le diagnostic d'HVG a été évaluée en utilisant les courbes de ROC. L'influence des caractéristiques des patients sur la performance du test a été évaluée avec une régression ROC basée sur un modèle spécifique. Quatre vingt treize sujets ont été inclus. Tous les sujets inclus avaient un NT-pro-BNP mesuré et ont bénéficié d'un électrocardiogramme, d'un échocardiogramme avec détermination de la masse ventriculaire gauche indexée (MVGI).

Résultats. — La performance diagnostique du NT-pro-BNP dans le diagnostic d'HVG varie en fonction du mode d'indexation de l'indice de masse ventriculaire gauche. En cas d'indexation à la surface corporelle, la surface sous la courbe ROC est à 81,6 %, suggérant une bonne performance diagnostique. La performance de ce marqueur est significativement plus élevée chez les femmes que chez les hommes ($p < 0,0001$). Il n'y avait pas de différence significative liée à l'âge, au traitement, à l'indice de masse corporelle, l'index de masse ventriculaire gauche, la pression artérielle systolique sur 24 heures ou la clairance de la créatinine sur la performance diagnostique. Des différences mineures ont été observées lorsqu'une indexation sur la taille à la puissance 2,7 a été utilisée et non la surface corporelle.

Conclusion. — Les résultats de cette étude pourraient conduire à une nouvelle stratégie de stratification du risque dans l'hypertension artérielle. Chez les femmes, le NT-pro-BNP isolé ou l'association à l'électrocardiogramme pourraient constituer une approche suffisante pour confirmer ou exclure le diagnostic d'HVG. Chez les hommes, l'échographie ne serait nécessaire qu'en l'absence d'HVG électrique avec un NT-pro-BNP négatif.

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Introduction

Left ventricular hypertrophy (LVH) in hypertension is a major predictor of cardiovascular events [1,2] and therefore has to be considered in the assessment of global cardiovascular risk [3]. In clinical practice, however, detection of LVH is subject to various limitations. Electrocardiography (ECG), recommended in most guidelines, has a poor sensitivity and is rarely performed in clinical practice [4]. Echocardiography is also extensively used but is time-consuming, expensive, and not always feasible for technical reasons. Thus the cost-effectiveness of systematic use of echocardiography in hypertensive patients is widely debated [5].

In response to volume expansion and pressure load, ventricular myocytes release a cardiac hormone, B-type natriuretic peptide (BNP), together with its N-terminal fragment, the N-terminal pro-brain natriuretic peptide (NT-proBNP) [6]. BNP levels are higher in hypertensive than normotensive patients [7]. Moreover, BNP is raised in LVH and in diastolic dysfunction [8]. Based on these findings, BNP levels could be related to cardiac remodeling in hypertension [9,10]. Despite these interesting features, the performance of BNP in the diagnosis of LVH is not sufficiently good to propose this marker for clinical use [11,12]. On the contrary, because of its longer half-life and lower intra-individual variability, the biologically inactive fragment NT-proBNP may offer some advantages in detecting subtle preclinical cardiac changes [13,14].

The aim of the present study was to assess the diagnostic value of NT-proBNP in the detection of LVH and

factors that may influence its performance in hypertensive patients.

Methods

Patients

One hundred and twenty-three consecutive patients referred to our cardiology department (hôpital de la Croix-Rousse, Lyon, France) for hypertension work-up were considered for inclusion. Exclusion criteria were systolic left ventricular dysfunction (shortening fraction [SF] < 25%), atrial fibrillation, and greater than mild valvular dysfunction. The study population for this analysis comprised 93 (76%) patients with a technically measurable left ventricular mass (LVM) on echocardiography.

Study protocol

In view of a work-up for hypertension, drugs interfering with hormonal regulations were withdrawn before hospitalization (six weeks for spironolactone; two weeks for diuretics, beta-blockers, and renin-angiotensin system inhibitors) and replaced by alpha-blockers or calcium antagonists as recommended [15].

Then, over a two-day hospital stay, all patients underwent 24-h ambulatory blood pressure measurement (ABP), ECG recording and echocardiographic assessment. While the 24-h ABP recording was in progress, a blood sample was taken after one night recumbence for NT-proBNP measurement and routine biological tests. All tests were part of the routine evaluation of hypertensive subjects.

ABP recording

Twenty-four hour ABP recordings used Spacelabs ABP monitors (Berkshire, UK), which satisfy the criteria of the British Hypertension Society (BHS) and the Association for the Advancement of Medical Instrumentation (AAMI) [16]. Systolic and diastolic ABP were recorded at 15-min intervals during the day (from 7:00 to 22:00) and at 30-min intervals during the night (from 22:00 to 7:00).

NT-proBNP measurement

Plasma concentrations of NT-proBNP were measured by an electrochemiluminescence immunoassay using an Elecsys 2010 analyzer (Roche Diagnostics, Meylan, France). The range of values was 5—35,000 pg/mL and the coefficient of variation was between 1 and 2.5% [17].

ECG criteria of LVH

ECGs were reviewed by an operator blinded to other data (AD). LVH was defined as at least one of the following: a Sokolow index ($SV_1 + RV_5 - V_6$) greater than 35 mm or a Cornell voltage criterion ($RVL + SV_3$) greater than 28 mm for men and greater than 20 mm for women [18].

Echocardiography

Two-dimensional images, M-mode, and Doppler recordings were obtained from a Vivid Five ultrasound device (GE Vingmed). Each parameter was recorded on three consecutive beats by the same experienced echocardiographist (C M-B), blinded to other data. LV dimensions were determined from M-mode images and were used to calculate LVM using the Devereux formula. The intra-observer variability for LVM calculation in our echocardiography laboratory is around 5% [19].

Two different indexations of LVM (LVMI) were used: (1) indexation to body surface area ($LVMI^{BSA}$) according to the European Society of Cardiology—European Society of Hypertension (ESC-ESH) guidelines with the following LVH criteria: LMI^{BSA} greater than 125 g/m^2 in men and greater than 110 g/m^2 in women [3], and indexation to height to the allometric power of 2.7 ($LVMI^{2.7}$) with the following LVH criteria: $LVMI^{2.7}$ greater than 51 g/m$^{2.7}$ in both sexes [20].

Different grades of diastolic function were defined according to previously published criteria [21—25] based on mitral flow, pulmonary venous flow, Color M-mode flow propagation velocity, and Doppler tissue imaging at the mitral annulus.

Data analysis

To assess the determinants of NT-proBNP, we used univariate analyses (Pearson's coefficient of correlation ''r'' and one-way analysis of variance) and a multivariable analysis (standard stepwise multiple linear regression). In addition to sex, treatment, and age, the independent variables tested in the multivariable analysis were those found significantly associated with NT-proBNP in univariate analyses. Because of skewed distributions, a logarithmic transformation was applied to NT-proBNP, LVMI and creatinine clearance values.

To estimate the global accuracy of NT-proBNP in diagnosing LVH, an empirical receiver-operating characteristic (ROC) curve was built. The area under the ROC curve (AUC) was estimated using the Mann—Whitney statistic and was compared to 50%. We used an ROC regression method [26] to quantify the effect of patients' characteristics on the accuracy of NT-proBNP. The method consisted of modelling an indicator that can show that the NT-proBNP results in patients with LVH are greater than specific quantiles of the marker distribution in patients without LVH but with the same characteristics. A generalised linear probit model was used for this binary outcome. Because of their documented importance or their association with NT-proBNP, we studied the effects of the following characteristics: age, sex, treatment, body mass index (BMI), 24-h systolic ABP, creatinine clearance, LVMI (for subjects with LVH).

The Youden index [27] was used to determine a positive threshold for NT-proBNP, then the corresponding positive (LR+) and negative (LR—) likelihood ratios were estimated. Post-test probabilities were calculated for a 30% estimated prevalence of LVH in primary care practice [28]. The analysis was carried out with the statistical software Stata, version 9.2. Each analysis was performed for both LVM indexations: $LVMI^{BSA}$ and $LVMI^{2.7}$.

Table 1 Patient characteristics ($n = 93$).

Characteristic	Men Mean [min;max] ($n = 51$)	Women Mean [min;max] ($n = 42$)	All Mean [min;max] ($n = 93$)
Age (years)	53.3 [20;76]	48.5 [22;75]	51.1 [20;76]
BMI (kg/m^2)	28.4 [21.6;45]	26.7 [16.9;41.0]	27.6 [16.9;45]
24-h systolic ABP (mmHg)	152.1 [114;210]	149.0 [105;220]	150.7 [105;220]
24-h diastolic ABP (mmHg)	91 [65;118]	89.7 [61;125]	90.4 [61;125]
Creatinine clearance (mL/min)	100.0 [47.3;214.1]	95.8 [45.5;167.6]	98.1 [45.5;214.1]
NT-proBNP (pg/mL)	224.7 [15.5;3911]	311.5 [10;3549]	264.3 [10;3911]
LVMI^{BSA} (g/m^2)	135.1 [64.8;248.5]	113.3 [47.4;248.5]	125.2 [47.4;248.5]
Shortening fraction (%)	39.2 [27;58]	37.9 [25;54]	38.6 [25;58]

BMI: body mass index; ABP: ambulatory blood pressure; LVMI^{BSA}: left ventricular mass indexed to the body surface area.

Results

The population comprised 42 women (45.2%) and 51 men (54.8%). The mean 24-h systolic ABP did not differ between sexes. Mean NT-proBNP was slightly higher in women, with a large variation in range from 10—3911 pg/mL in both sexes (Table 1). Overall, 76.3% of patients received the antihypertensive regimen described above, with a higher rate of treatment in men (90%) than in women (63%). Creatinine clearance, calculated using the Cockcroft formula, was found to be less than 60 mL/min in 4.3% of the patients; none had a creatinine clearance below 30 mL/min. The prevalence of LVH using the BSA indexation criterion (LVH^{BSA}) was 44% (that is, fourfold that determined by ECG, 11%). The prevalence of LVH using the height to the allometric power of 2.7 indexation criterion (LVH$^{2.7}$) was 53%. Diastolic function could not be estimated in 21 patients because of discrepant indices, leaving 72 patients (77%) classified as follows: 40% normal, 43% impaired relaxation, and 17% pseudonormal pattern.

Determinants of NT-proBNP

In the multivariable analysis LVMI^{BSA}, 24-h systolic ABP and sex were independent determinants of NT-proBNP (Table 2).

Table 2 Effect of patient characteristics on NT-proBNP level: multiple linear regression model.

Characteristic	Regression coefficient	p-value
Age	−0.002	0.99
Women vs men	0.26	0.04
Treatment	0.025	0.84
Log creatinine clearance	−0.09	0.54
24-h systolic ABP	0.46	0.003
Log LVMI^{BSA}	0.40	0.02
Diastolic dysfunction (1, 2, 3 for normal, moderate, severe dysfunction)	0.07	0.69

ABP: ambulatory blood pressure; log LVMI^{BSA}: log left ventricular mass indexed to body surface area.

The mean NT-proBNP value was significantly higher in women than in men and the value increased when creatinine clearance decreased. Conversely, the NT-proBNP value increased when the 24-h systolic ABP and LVMI^{BSA} values increased. Similar findings were obtained for LVMI$^{2.7}$.

Accuracy of NT-proBNP for diagnosing LVH

The accuracy of NT-proBNP in identifying patients with LVH^{BSA} (Fig. 1) was high; estimated AUC 81.6% (95% confidence interval 72—91). This AUC can be interpreted as the probability that the NT-proBNP value of a patient with LVH^{BSA} is greater than that of a patient without LVH^{BSA}.

The results of the ROC regression showed that the accuracy of the NT-proBNP for the diagnosis of LVH^{BSA} was dependent on the patients' characteristics (Table 3). After adjustment for the other patients' characteristics, the accuracy was significantly higher in women than in men ($p < 0.0001$) and the difference between women and men increased along with the false-positive rate ($p < 0.001$; Table 3 and Fig. 2). Treatment tended to decrease the accuracy of the marker but the difference was not statistically
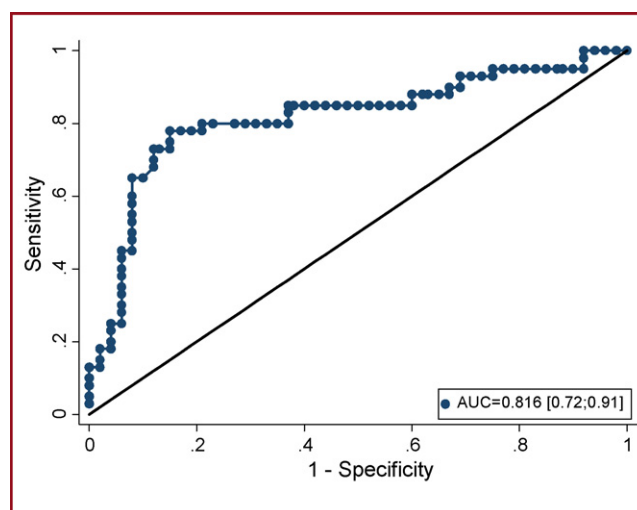

Figure 1. ROC curve of the NT-proBNP test used to identify left ventricular hypertrophy according to body surface area indexation (LVH^{BSA}).

Table 3   Effect of patient characteristics on ROC curve of NT-proBNP for diagnosis of LVH^{BSA}: ROC regression model.

Characteristic	Regression coefficient	95% confidence interval	*p*-value
Women vs men	2.19	[1.05;3.34]	< 0.0001
Interaction between sex and false positive rate	1.38	[0.57;2.19]	< 0.001
Age	0.013	[−0.03;0.05]	0.66
BMI	0.09	[−0.01;0.19]	0.09
Creatinine clearance	−0.01	[−0.03;0.003]	0.12
24-h systolic ABP	0.01	[−0.005;0.026]	0.18
LVMI^{BSA}	0.008	[−0.003;0.02]	0.15
Antihypertensive treatment	−0.8	[−1.75;0.15]	0.1
False positive rate	1.02	[0.78;1.28]	< 0.0001

BMI: body mass index; ABP: ambulatory blood pressure; LVMI^{BSA}: left ventricular mass indexed to body surface area.

significant (Table 3). With the other patients' characteristics fixed to their mean (Table 1), the adjusted AUC was estimated at 96% in treated women and 68% in treated men (Fig. 2A) whereas it was 99% in untreated women and 85% in untreated men (Fig. 2B). Age had no effect on
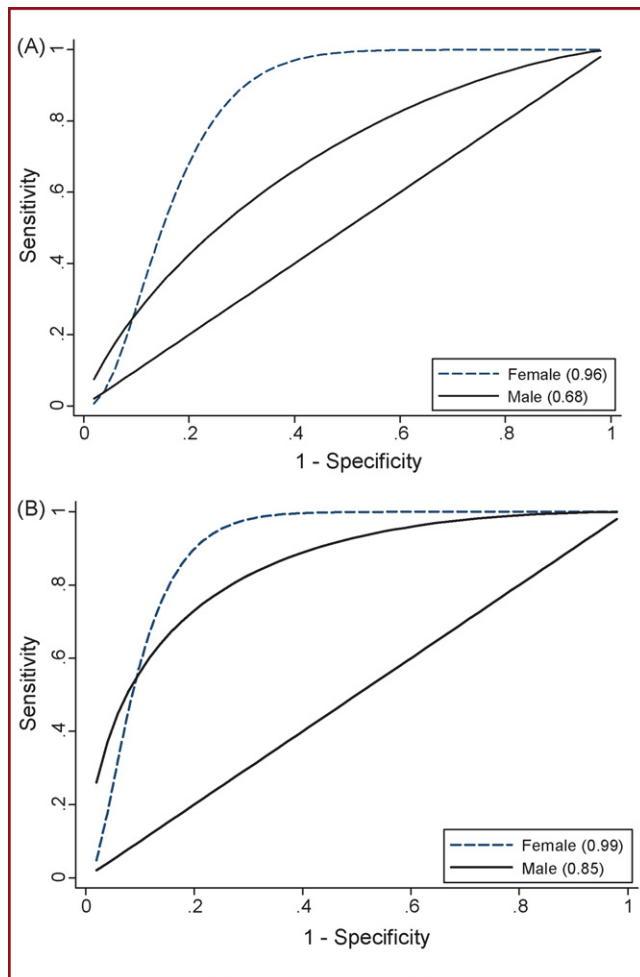

Figure 2.   Adjusted ROC curves of the NT-proBNP test used to identify left ventricular hypertrophy according to body surface area indexation (LVH^{BSA}), sex, and other patients' characteristics in (A) treated and (B) untreated men and women. Corresponding AUC values are in brackets.

the accuracy of the marker (Table 3). Accuracy tended to increase along with increasing BMI (Fig. 3A), 24-h systolic ABP (Fig. 3B) and LVMI^{BSA} in patients with LVH^{BSA}, and with the decrease in creatinine clearance (Fig. 3C). However, the four above-mentioned effects did not reach statistical significance (Table 3).

When considering LVH$^{2.7}$, test performance was slightly worse, with an estimated AUC of 73.8% (95% confidence interval 63−84). The results of the ROC regression were similar to the other indexation of LVM with a marked effect of sex (Fig. 4). The trends observed for BMI and creatinine clearance reached statistical significance.

The thresholds determined by the Youden index for LVH^{BSA} were 111 pg/mL in men and 144 pg/mL in women, with the corresponding performances indicated in Table 4 (the diagnostic performances of the retained ECG criteria are also given for comparison). ECG was a powerful marker of confirmed LVH^{BSA} diagnosis, with 100% specificity in our study, but had a poor performance in excluding that diagnosis. NT-proBNP appeared to be a more balanced test with a good ability to confirm LVH^{BSA} in both sexes (LR+ between 7 and 8) and an excellent ability to exclude the diagnosis in women. For example, in women with a pre-test probability of 30% (prevalence of LVH), the probability of LVH^{BSA} decreased to 5% when the biological test was negative versus 25% when the ECG was negative. When electrocardiographic and biological markers were combined, the gain in ability to exclude LVH^{BSA} when the two tests were negative was only marginal: LR = 0.10 in women and 0.32 in men with the two markers versus 0.13 in women and 0.41 in men with NT-proBNP alone. That combination had a modest impact on the probability of LVH^{BSA}: 4% versus 5% in women, 12% versus 15% in men, for a 30% pre-test probability.

When indexation to height raised to the allometric power of 2.7 ($h^{2.7}$) was used, the Youden index was maximal for the same NT-proBNP value of 144 pg/mL in women. For men, it was maximal for an NT-proBNP value of 82.4 pg/mL.

Discussion

The major findings from this study were the good performance of NT-proBNP in diagnosing LVH in hypertensive patients, and the impact of sex on the test, with a much better diagnostic value in women than in men. These findings

Table 4 Likelihood ratios of ECG and NT-proBNP for a threshold of 111 pg/mL in men and 144 pg/mL in women, and probability of LVH^{BSA} according to results in a population with a 30% prevalence of LVH.

Test	Sensitivity (95% CI)	Specificity (95% CI)	LR+ (95% CI)	Probability of LVH when the test is positive	LR− (95% CI)	Probability of LVH^{BSA} when test is negative
NT-proBNP						
Men	0.62 (0.40;0.81)	0.93 (0.76;0.99)	8.43 (2.53;31.23)	0.78 (0.52;0.93)	0.41 (0.23;0.63)	0.15 (0.09;0.21)
Women	0.88 (0.63;0.98)	0.88 (0.69;0.97)	7.35 (2.86;21.40)	0.76 (0.55;0.9)	0.13 (0.04;0.40)	0.05 (0.02;0.15)
ECG						
Men	0.25 (0.09;0.47)	1 (0.83;1)	—	—	0.75 (0.56;0.93)	0.24 (0.19;0.28)
Women	0.23 (0.07;0.50)	1 (0.83;1)	—	—	0.76 (0.54;0.96)	0.25 (0.19;0.29)

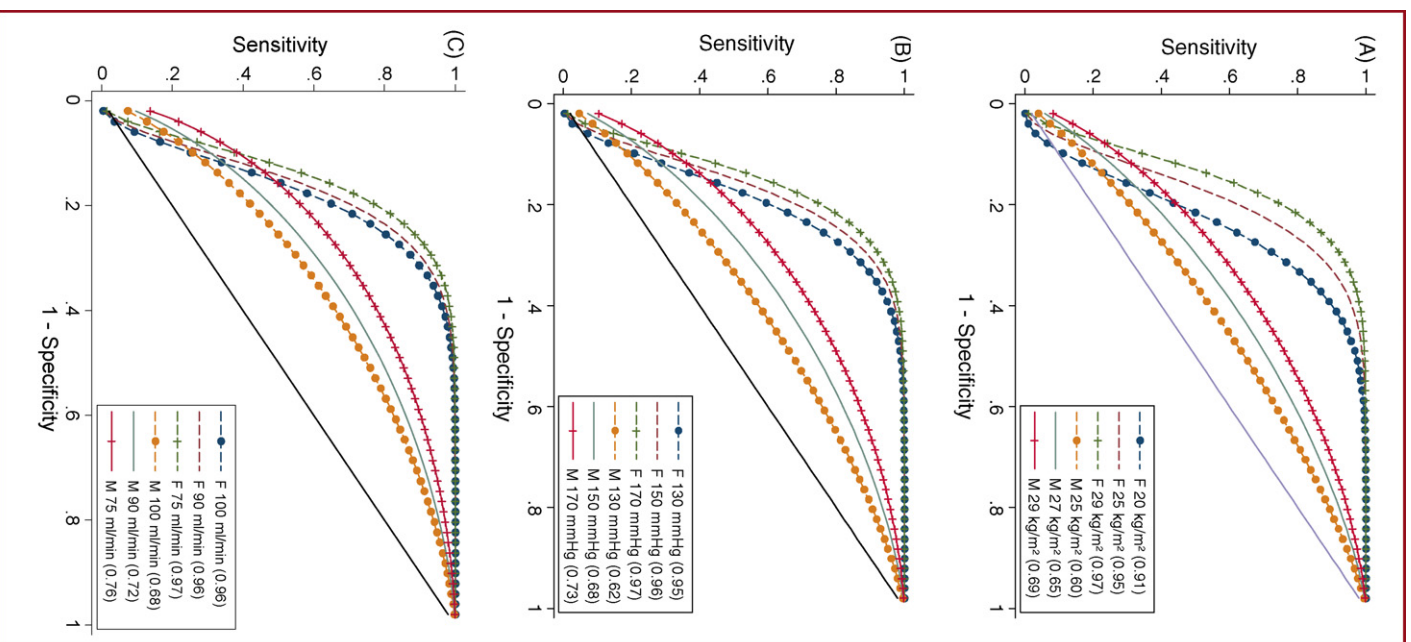LR+: positive likelihood ratio; LR−: negative likelihood ratio.

Figure 3. Adjusted ROC curves of the NT-ProBNP test used to identify left ventricular hypertrophy according to body surface area indexation (LVH^{BSA}) for treated women and men, for (A) body mass index, (B) 24-h systolic ambulatory blood pressure, and (C) creatinine clearance. Corresponding AUC values are in brackets.

may have important clinical implications for cardiovascular risk assessment in hypertension.

In accordance with previous reports [7,12,29—31], NT-proBNP was associated with LVMI even after taking into account important confounders including diastolic dysfunction [32], renal function and sex. More importantly, the ROC curve analysis showed a good accuracy of NT-proBNP
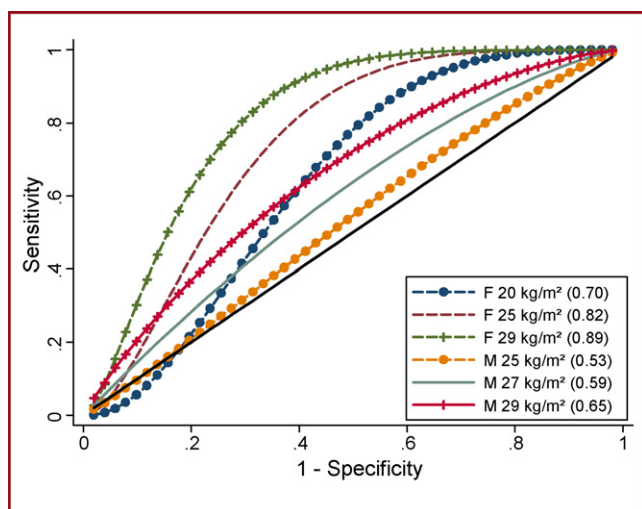
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Figure 4. Adjusted ROC curves of the NT-ProBNP test used to identify left ventricular hypertrophy according to height$^{2.7}$ indexation for treated women and men for different values of body mass index. Corresponding AUC values are in brackets.

in detecting LVH^{BSA} with an AUC of 81.6%, supporting the diagnostic value of this biomarker.

Until now, few studies have evaluated natriuretic peptides for the diagnosis of LVH, and most gave rather negative results. Besides, in three studies conducted in hypertensive patients, the performance of BNP alone was suboptimal [11,12,33]. This might be due to the high intra-individual variability [13] and short half-life [14] of this marker: two features that impact the ability of BNP to detect subtle cardiac variations such as those occurring in hypertension. Indeed, NT-proBNP seems more closely related to LVH than BNP in a study by Belluardo et al. [34]; of note, in this study like in ours, a major effect of blood pressure on peptide levels was disclosed. Concerning the diagnostic value of NT-proBNP, in a study performed in a large sample from the general population in which the prevalence of LVH was low, the authors reported a lower diagnostic performance than ours [35]. This may be explained by differences in the way in which natriuretic peptides were measured, in the criteria required to calculate LVM or by the inclusion of patients with systolic dysfunction.

The use of a ROC regression based on a probit model allowed us to quantify the effect of patients' characteristics on the accuracy of NT-proBNP. The most striking effect was that of sex, with a significantly higher accuracy in women than in men, found with both LVM indexations, LVMI^{BSA} and LVMI$^{2.7}$. This effect has not been reported so far for LVH but is in agreement with the higher prognostic value of this marker in women referred for acute dyspnoea [36]. A likely explanation could be the ''BNP handicap'' evoked in men: under testosterone influence, myocytes in men seem to produce less natriuretic peptide than those in women [37]. The lower hypertrophic reserve in men may also contribute to a lower release of BNP [38]. It has been speculated that the decoupling between cardiac mass and natriuretic peptide synthesis might initiate a vicious circle, leading more rapidly to heart failure. Our results currently support the hypothesis that early cardiac impairment, such as LVH, is more closely related to NT-proBNP in women than in men. On

the contrary, the difference in use of antihypertensive therapy in men and women is an unlikely explanation because treatment did not significantly affect the accuracy of the test.

In accordance with previous reports [39,40], neither age nor modest renal impairment affected the performance of the biomarker. The effect of BMI modified the capacity in case of $h^{2.7}$ indexation but the accuracy increased along with the increase of BMI. In the common clinical scenario of overweight hypertensive patients, the test could still therefore prove useful.

Finally, the population in the present study had a relatively high prevalence of LVH [41]. Interestingly, neither hypertension severity nor LVMI level seemed to markedly affect the performance of NT-proBNP. All of these characteristics strongly suggest that the diagnostic performance of this marker would be the same in primary care hypertensive patients.

One possible limitation concerns our ''gold standard''. Indeed, although considered as the reference method, echocardiography has a high rate of failure and a limited reproducibility. However, LVMI was measured carefully by a single operator to avoid inter-operator variability. In addition, only patients with technically optimal recordings were included in the study to improve the accuracy of the determination. Finally, despite the relatively small study population, the results were rather clear, especially the highly significant effect of sex.

In hypertensive women, NT-proBNP alone or preferably in combination with ECG appeared sufficiently efficient in confirming or excluding the diagnosis of LVH without the necessity for further investigations. Indeed, when using LVMI^{BSA} indexation and for a pre-test probability of 30% [28], the negative post-test probability would decrease to 5% with only a marginal improvement of the test performance by adding ECG. Similarly, the positive post-test probability would rise to 76% and would approach 100% by adding ECG. This approach suggests that cardiac risk stratification could be based on only these two markers in hypertensive women, with an acceptable risk of false positives and negatives.

The picture is similar in cases of a positive test in men. However, in those with a negative test, the post-test probability would still be high, around 12%, which may not be sufficient to exclude the diagnosis. Thus, the optimal approach would be to perform an echocardiography in men with a negative ECG and a negative NT-proBNP test.

The combination of NT-proBNP and another diagnostic test has already been proposed to increase the performance of each test. For example, the combination of C-reactive protein (CRP) and BNP yielded a 99% negative predictive value, suggesting that this approach could be sufficient to exclude LVH without further investigation [33]. Two points deserve special emphasis in our study: first, the ECG is part of the routine evaluation recommended in most guidelines and is not associated with extra costs; second, the performance appeared much better in women than in men, which was not tested in the aforementioned study [33].

Finally, some recent results suggest that the value of natriuretic peptides may go beyond cardiac impairment. McKie et al. [42] tested the predictive value of these peptides in a population free of heart failure. They showed that, with a threshold at 109 pg/mL, a high NT-proBNP was pos-

itively related to prognosis. A similar predictive value was also demonstrated by Wang et al. [43].

In our study the thresholds were determined by the Youden index, which is a debatable choice. They may be refined according to the prevalence of LVH in the target population and to the diagnostic strategy by choosing a high sensitivity or a high specificity. However, the fact that these thresholds were very similar to those obtained in prognostic studies [42,43] strengthens their relevance and extends their clinical interest beyond the detection of LVH.

Conclusions

Our study shows that, in addition to ECG, NT-proBNP may prove to be a useful routine screening test for LVH in hypertensive patients. This biomarker has the advantages of being both easy to obtain in all patients and affordable. In our study, this strategy proved extremely valuable in women, while it may limit the need for echocardiography in men with a negative ECG and negative NT-proBNP. This has to be checked in other groups of hypertensive patients with a different prevalence of LVH. It also has to be confirmed with magnetic resonance imaging determination of LVH, which would be more relevant. Taken as a whole, the present results open the way for a new strategy of risk stratification in hypertension.

Acknowledgements

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