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Abstract

Introduction :

Pheochromocytomas and paragangliomas (PPGLs) are rare neuroendocrine tumors arising from chromaffin cells of the adrenal medulla or from sympathetic and parasympathetic ganglia. Their heterogeneous clinical presentation often leads to diagnostic delay and exposes patients to significant cardiovascular morbidity.

Methods:

We conducted a retrospective, descriptive, and analytical study over a 20-year period (2004–2024) in the Department of Endocrinology and Diabetology of Ibn Ziri Public Hospital, Algiers. Patients hospitalized for confirmed PPGLs were included. Clinical, biochemical, imaging, genetic, histopathological, and follow-up data were analyzed.

Results:

Sixty-eight patients were included (mean age 39 ± 15.7 years). Incidental discovery was the most frequent mode of presentation (52.9%). Arterial hypertension was present in 69.1% of patients, including resistant hypertension in 29.8%. Diabetes mellitus was observed in 30.8%. Cardiovascular complications occurred in 35.3%, mainly left ventricular hypertrophy. Tumors were of moderate size (mean diameter 63.5 ± 30.4 mm), with bilateral involvement in 20.6%. Pathogenic genetic variants were identified in 32.4%. Malignancy was confirmed in 14.7% of cases. Post-treatment, blood pressure normalized in 60% of patients and glycemic control improved in 46.6%.

Conclusion:

PPGLs are most frequently diagnosed incidentally in our cohort. Cardiovascular complications remain common and potentially severe. Our findings are consistent with existing literature and highlight the importance of early diagnosis and multidisciplinary management.

1. Introduction

Pheochromocytomas and paragangliomas (PPGLs) are rare neuroendocrine tumors arising from catecholamine-secreting chromaffin cells, located in the adrenal medulla in approximately 80–85% of cases, and in sympathetic or parasympathetic ganglia in the remaining 15–20%. [1]The estimated incidence of PPGLs is around 0.57 per 100,000 person-years. [2] Nearly 40% of cases are attributable to genetic mutations and may occur as part of various hereditary syndromes. [3]Malignant transformation occurs in approximately 10–17% of cases. [3]

The clinical presentation is primarily driven by catecholamine excess, most commonly manifesting as hypertension. Diagnosis relies on elevated plasma or 24-hour urinary metanephrines and is confirmed by imaging studies to localize the tumor. Surgical resection remains the mainstay of initial management and should be as complete as possible. [4]

PPGLs carry a considerable risk of mortality, predominantly due to cardiovascular complications. [5, 6] Increasingly, pheochromocytomas are being identified incidentally during imaging performed for unrelated reasons—so-called adrenal incidentalomas—accounting for 3.9% to 59.8% of cases in recent series, largely due to advancements in and broader access to modern imaging techniques. [7–9]

In light of the evolving patterns of presentation, the aim of this study was to assess the proportion of incidentally discovered pheochromocytomas and to compare their clinical, biochemical, and radiological characteristics with those of tumors identified through adrenergic symptoms and/or uncontrolled hypertension.

2. Objectives of the study

The objective of this study is to describe the epidemiological, clinical, biochemical, radiological, therapeutic, and outcome profiles of pheochromocytomas and paragangliomas managed in our institution, with a particular focus on comparing cases based on their mode of presentation.

3. Materials and Methods

3.1. study methodology:

This retrospective, descriptive, and analytical study included patients hospitalized for pheochromocytomas and paragangliomas in the Department of Endocrinology and Diabetology at the Ibn Ziri Public Hospital (EPH), located in Bologhine, Algiers, Algeria, over a 20-year period (2004–2024).

The diagnosis was established either histologically or through the combined presence of elevated plasma-free and/or urinary fractionated metanephrines (metanephrine, normetanephrine, and 3-methoxytyramine), along with imaging evidence of an indeterminate adrenal mass (on CT or MRI) and positive uptake on meta-iodobenzylguanidine (MIBG) scintigraphy.[10, 11]

Data were extracted from patient records using a standardized data collection form that included anamnesis, clinical presentation, biochemical findings, imaging results, therapeutic management, and disease course.

Postoperative follow-up was conducted at regular intervals, using both biochemical markers and imaging to monitor recurrence or progression. Operative reports and intraoperative monitoring records were systematically reviewed.

3.2. Biological assessment:

Potential drug-induced interferences leading to false-positive elevations of methoxylated derivatives were systematically ruled out in all cases. [12]

For the measurement of plasma-free metanephrines, blood samples were collected after the patient had been in a supine position for at least 30 minutes, using pre-chilled heparinized tubes. [13] In the case of 24-hour urinary fractionated metanephrines, samples were collected in acidified containers (to maintain urinary pH below 4) and stored under refrigerated conditions. Urinary creatinine levels were used to validate the completeness of the collection. [10]

Metanephrine (MN) levels in both plasma and urine were quantified using liquid chromatography–tandem mass spectrometry (LC-MS/MS). [10]

All patients underwent hormonal assessment both before and after surgery, with data obtained from hospital records and documented via a standardized questionnaire. Until 2018, biochemical evaluation was based on 24-hour urinary metanephrines; since 2018, plasma metanephrine testing was introduced, offering enhanced sensitivity and specificity. [14]

3.3. Morphological assessment:

Imaging modalities—including computed tomography (CT), magnetic resonance imaging (MRI), and iodine-123 meta-iodobenzylguanidine (^{123}I-MIBG) scintigraphy—were employed based on clinical indications and resource availability.

3.4. Genetic testing:

With informed patient consent, genetic testing was conducted in accordance with national eligibility criteria, targeting mutations in the RET (NM_020975), SDHD (NM_003002.4), and VHL (NM_000551.2) genes. [15] Due to technical constraints, genetic analysis could not be performed for all patients. The diagnosis of neurofibromatosis type 1 (NF1) was established based on the presence of characteristic clinical criteria.

3.5. Statistical analysis:

Metanephrine (MN) levels were expressed as multiples of the upper limit of normal (ULN), with a value of zero assigned when no elevation was detected. For analysis, the largest tumor diameter and the highest MN or normetanephrine (NMN) concentration—regardless of whether measured in plasma or urine—were used. In patients with bilateral pheochromocytoma, only the largest lesion was considered.

Statistical analyses were performed using Microsoft Excel for Windows 10, version 2021. Categorical variables were reported as percentages, while continuous variables were presented as means with standard deviations (SD). Comparisons between means were conducted using Student’s t-test. Correlations between variables were assessed using Excel’s CORREL function. A p-value less than 0.05 was considered statistically significant.

4. Results

4.1. Epidemiological characteristics:

In our cohort, a marked female predominance was observed, with 69.1% of cases occurring in women compared to 30.8% in men, corresponding to a female-to-male ratio of 2.2. The mean age at diagnosis was 39 ± 15.74 years, with ages ranging from 13 to 76 years (Table 1).

Table 1. Patient characteristics

Characteristic	Result
Sex, N (%)	68
· Male	21 (30.8)
· female	47 (69.1)
BMI (kg/m²)	24
Mean age at diagnosis, y ± SD	39 ± 15.74
Mode of presentation, N (%)	
· adrenal incidentaloma	36 (52.6)
· Family screening	12 (17.6)
· Menard's triad	07 (10.29)
· Hypertension in young patients	09 (13.2)
· Resistant hypertension	04 (5.8)
Comorbidities and complications, N (%)	47 (69.1)
· Hypertension	21 (30.8)
· Diabetes mellitus	24 (35.29)
· Cardiovascular complications:	17
- Left ventricular hypertrophy	01
- Ischemic cardiomyopathy	01
- Hemorrhagic stroke	03
- Hypertensive retinopathy	01
- Takotsubo syndrome	01
- Cardiac arrhythmia (Wolff–Parkinson–White type)	
Menard's triad, N (%)	32 (47.05)
Metastatic disease at presentation, N (%)	02
Biochemical diagnosis, N (%)	
· Elevated methoxylated derivatives	62 (91.17)
- Mixed secretion	36 (58.06)
- Normetanephrine increased only	18 (29)

- Metanephrine increased only	07 (11)
- 3-O-methyldopamine increased only	01 (1.6)
· All values normal / No elevation	06 (8.8)
Morphological characteristics	
· Mean tumor size (mm) ± SD (range)	63.47 ± 30.44 (10-150)
· Mean unenhanced density (Hounsfield Units) ± SD (range) (reported in 36.76% of cases)	39.76 ± 17.62 (14-98)
- ≤ 10 UH	
- ≤ 20UH	0 boxes
- >20 UH	03 boxes
· Heterogeneous appearance, N (%)	22 boxes
· Signs of necrosis, N (%)	
· Presence of calcifications, N (%)	26 (38.23)
· Hemorrhage, N (%)	23 (33.8)
· Bilateral tumors, N (%)	07 (10.29)
	02 (2.9)
Preoperative medical preparation, N (%)(remaining not specified)	14 (20.58)
· α-blockers	
- Prazosin	42 (82.35)
- Doxazosin	36 (85.71)
- Combined with β-blockers	07 (19.44)
· Calcium channel blockers	29 (80.55)
Histopathological characteristics	24 (66.6)
· PASS score, number of cases specified (%)	06 (14.28)
- Mean PASS score	
- PASS < 4	
- PASS ≥ 4	22 (36.06)
· Ki-67 index, number of cases specified (%)	4.9
- Mean Ki-67 index	10
- Ki-67 < 3%	12
- Ki-67 ≥ 3%	

Metastases, N	14 (22.95)
Recurrences, N	4.38
Deaths, N	09
	05
	10
	01
	01

Abbreviations: BMI: Body Mass Index; PASS: Pheochromocytoma of the Adrenal gland Scaled Score.

4.2. Clinical features:

In our series, pheochromocytomas were most often incidentally discovered as adrenal incidentalomas (52.9%). Other contexts included family screening (17.6%), hypertension in young patients (13.2%), Ménard's triad (10.29%), and resistant hypertension (5.8%) (Table 1).

Among patients with incidentally diagnosed tumors, imaging was initially performed for various reasons: abdominal symptoms in 72.2% (abdominal pain: n = 23)hematologic investigation for anemia (2.7%), urological evaluation (urinary lithiasis: 5.5%), gynecological workup (2.7%), or in the context of metastatic bone lesions (5.5%). Ménard's triad comprising headache, sweating, and palpitations—was observed in 47.05% of patients.

Complications: Arterial hypertension was present in 69.1% of cases, with a mean duration of 4 years. Among these, 14 patients had resistant hypertension. Additionally, diabetes mellitus was reported in 30.8% of patients (Table 1).

Cardiovascular complications were identified in 35.29% of cases and included the following: left ventricular hypertrophy (n = 17), ischemic cardiomyopathy (n = 1), hemorrhagic stroke (n = 1), hypertensive retinopathy (n = 3), Takotsubo cardiomyopathy (n = 1), and a cardiac conduction abnormality (Wolff-Parkinson-White syndrome; n = 1).

4.3. Secretory characteristics:

In our series, urinary methoxylated derivatives were the primary diagnostic modality, performed in 69.1% of cases, compared to 30.8% for plasma assays. A gradual shift toward plasma-based testing was noted from 2018 to 2020, reflecting its superior sensitivity and specificity. [14]

Methoxylated derivative (MD) assays were positive in 91.17% of cases, indicating a high diagnostic yield. Among positive results, the most frequent secretion profile was combined elevation of both normetanephrines and metanephrines (58.06%), followed by isolated normetanephrine elevation (29%), isolated metanephrine elevation (11%), and a rare profile with elevated 3-methoxytyramine (1.6%) (Table 1).

Among patients with positive results, 93.5% showed MD levels exceeding three times the upper limit of normal, a threshold strongly suggestive of pheochromocytoma. In contrast, 6.5% presented moderate elevations (< 3× ULN); all of these were familial cases associated with multiple endocrine neoplasia type 2A (MEN2A), subsequently confirmed by genetic testing.

Conversely, six patients (8.8%) had negative MD assays. Surgical intervention was indicated in four of these based on radiological suspicion of adrenal incidentalomas, and in two others due to intercarotid paragangliomas diagnosed at the metastatic stage.

4.4. Morphological characteristics:

Computed tomography (CT) was performed in the vast majority of patients (97.05%; n = 66), with the exception of two pregnant women who underwent magnetic resonance imaging (MRI). The mean tumor diameter was 63.47 ± 30.44 mm. Mean unenhanced attenuation was reported in 36.76% of cases, with an average of 39.76 ± 17.62 Hounsfield units (HU) (range: 14–98) (Table 1).

None of the patients had a spontaneous density ≤ 10 HU, a threshold generally considered to rule out pheochromocytoma [16, 17]. Only three patients had a density ≤ 20 HU, while the majority (n = 22) exceeded 20 HU, in line with current diagnostic guidelines.

Morphologically, tumor heterogeneity was frequently observed (n = 26). Additional features included necrotic areas in 23 patients (33.8%), calcifications in 7 patients (10.29%), and hemorrhagic changes in 2 cases (2.9%). Bilateral adrenal involvement was identified in 14 patients (20.58%).

^{123}I-MIBG scintigraphy was performed in 17.64% of patients and was particularly useful for assessing atypical or potentially malignant lesions. This included 5 patients with MEN2A-associated pheochromocytomas, 6 cases of malignant pheochromocytomas or paragangliomas, and large bilateral tumors (> 10 cm). This selective use aligns with current recommendations [10], which advocate functional imaging for high-risk or advanced forms.

Correlation Between Tumor Size and Metanephrine Levels:

A significant positive correlation was observed between tumor size and plasma metanephrine levels (**R = 0.19; P < 0.001**) (Fig. 1), suggesting that larger tumors are associated with higher catecholamine secretion.

4.5. Familial pheochromocytoma:

In our cohort, familial pheochromocytoma was found in 22 patients (32.35%). Hereditary cases were mainly MEN2A (61.9%, n = 13) with **RET** mutations, followed by neurofibromatosis type 1 (23.8%, n = 5). **VHL** syndrome was confirmed in 3 patients (14.28%), and one patient (4.5%) carried a pathogenic **SDHD** mutation.

4.6. Comparison between sporadic and hereditary pheochromocytoma:

Hereditary pheochromocytoma cases were diagnosed at a significantly younger age than sporadic cases (**34 ± 13.31 vs. 41 ± 16.38 years; P = 0.020**) and showed a higher frequency of bilateral adrenal involvement (**57.14% vs. 4.2%; P = 0.040**). No significant differences were observed regarding arterial hypertension, Ménard's triad, or mean tumor size (Table 2). Genetic testing was not systematically performed in all patients.

Table 2
Comparison between sporadic and hereditary pheochromocytoma.

	sporadic form (N = 46)	Hereditary form (N = 22)	P-value
Number of patients (M/F)	11/35	10/12	P = 0.020
Mean age (years) ± SD	41 ± 16.38	34 ± 13.31	
Hypertension (number of patients) (%)	34 (73.91%)	13 (59.09%)	P = 0.120
Menard's triad (%)	23 (50%)	09 (40.9%)	P = 0.120
Tumor size ± SD (mean in mm)	63.64 ± 27.33	64.95 ± 37.63	
Bilaterality	02 (4.2%)	12 (57.14%)	P = 0.440
			P = 0.040

Characteristics of patients with pheochromocytomas according to the mode of discovery:

After excluding patients diagnosed by genetic screening (N = 12; 17.6%), two subgroups were defined: Group 1, with incidental adrenal incidentaloma discovery (64.28%), and Group 2, diagnosed due to adrenergic symptoms and/or uncontrolled hypertension (35.7%) (Table 3).

Table 3
patient characteristics according to the mode of discovery.

	Adrenal incidentaloma	Hypertension/Adrenergic signs	P-value
Number of patients, N (%)	36 (64.28%)	20 (35.7%)	P = 0.003
Median age at diagnosis, years (range)	49.5 (16–76)	31 (17–66)	P = 0.020
Median tumor diameter: mm (range)	65.75 (22–150)	55.5 (36–90)	P = 0.100
Increase in MN LSN (median)	9.32x LSN	10x LSN	
Hypertension, N (%)	26 (72.2)	-	
Adrenergic symptoms, N (%)	22 (61.1)	-	
The captions of the figures:			

Group 1 patients were older (median 49.5 years) than Group 2 (31 years, p = 0.003) and had larger tumors (median 65.75 mm vs. 55.5 mm, p = 0.020), suggesting delayed diagnosis. No significant difference was found in catecholamine secretion (p = 0.100).

Retrospectively, 61.1% of Group 1 had prior adrenergic symptoms, and 72.2% had hypertension before diagnosis (Table 3).

4.7. Preoperative medical preparation:

Preoperative pharmacological preparation was documented in 82.35% of patients (n = 56). In the remaining 17.65%, details regarding the preparatory regimen were not specified in the medical records.

Two primary therapeutic strategies were identified. The first and most frequently employed approach involved the use of α-adrenergic blockers, prescribed in 85.71% of prepared patients (n = 36). Among these, doxazosin was the most commonly administered agent (80.55%; n = 29), followed by prazosin (19.44%; n = 7). The mean daily dose of doxazosin was 3.17 mg, with a range of 1 to 16 mg.

In 66.6% of patients receiving α-blockade (n = 24), a β-blocker was introduced from the third day of treatment, primarily to manage newly developed or exacerbated tachycardia.

The second strategy involved the use of calcium channel blockers, prescribed in 14.28% of cases (n = 6). This approach was more frequently observed in earlier cases, prior to the routine implementation of α-blockers as standard preoperative therapy.

4.8. Surgical management:

Among the 68 patients included in this study, 61 (89.67%) underwent adrenalectomy. An open surgical approach (laparotomy) was employed in the majority of cases (86.8%; n = 53), likely reflecting the

relatively large average tumor size observed in our cohort (65.7 mm). A laparoscopic approach was utilized in 13.11% of cases (n = 8).

Surgery was not performed in three patients (4.41%) due to the presence of metastatic disease at diagnosis, which rendered curative intervention inappropriate. At the time of analysis, four additional patients were still awaiting surgical treatment.

Postoperative outcome data were not available for inclusion in this report.

4.9. Histopathological characteristics:

Histological examination confirmed the diagnosis of pheochromocytoma or paraganglioma in all analyzed cases.

The Pheochromocytoma of the Adrenal gland Scaled Score (PASS) was reported in 36.06% of patients (n = 22), with a mean score of 4.9. Among these, 54.5% (n = 12) had a PASS ≥ 4, indicating a higher risk of malignant potential, while 45.5% (n = 10) had a PASS < 4 (Table 1).

The Ki-67 proliferation index was available for 14 patients (22.95%), with a mean value of 4.38%. In this group, 9 patients had a Ki-67 index below 3%, whereas 5 patients had a value ≥ 3%, a threshold commonly used to distinguish more aggressive tumors.

A total of 10 metastatic cases were recorded. One patient experienced a local recurrence on the ipsilateral side, occurring 7 years after the initial surgery. One death was reported during follow-up; it involved a metastatic, initially inoperable pheochromocytoma.

4.10. Post-operative development:

Among the 35 patients with preoperative arterial hypertension, blood pressure normalization was achieved in 21 cases (60%). Antihypertensive treatment could be reduced in 12 patients (34.2%), while persistent hypertension was observed in only 2 cases (5.7%).

In terms of glucose metabolism, of the 21 patients with preoperative diabetes, normalization of glycemic control was noted in 7 individuals (46.6%). An improvement allowing for treatment reduction was reported in 3 cases (20%), while diabetes remained persistent in 5 patients (33.3%) (Fig. 2).

5. Discussion

Our study confirmed a marked female predominance (69.1%), similar to reports from several international series. [18–20] However, other studies from India and the United Kingdom reported a more balanced sex distribution, suggesting possible geographic or genetic influences.[19, 21]

The mean age at diagnosis was 39 ± 15.74 years, slightly younger than that reported by Zouihri et al. (42.5 years) and Noblet-Dick et al. (44.6 years). [18, 19] This difference may reflect earlier detection of hereditary or syndromic cases.

In our study, adrenal incidentalomas accounted for 52.9% of diagnoses, higher than earlier reports but comparable to more recent series, highlighting the increasing role of imaging in tumor detection. [8–10]

Menard's triad was documented in 47.05% of cases, in line with the rate reported by Noblet-Dick et al. (50%), but markedly lower than that of Zouihri et al. (84.6%), suggesting a progressive decline in typical symptomatic presentations due to more frequent incidental finding. [19, 18]

The role of familial screening was notable in our cohort, contributing to 17.6% of diagnoses, underlining the importance of considering genetic predisposition, especially in early or bilateral forms.

Cardiovascular complications were present in about 35% of cases, consistent with previous reports. [20]

Arterial hypertension was noted in 69.1% of patients, including 14 cases of resistant hypertension. While slightly lower than the rates reported by Noblet-Dick (80%) and Lu (94.7%), it remains comparable to those in the Moroccan (73.1%) and Spanish (77.7%) cohorts. [18, 19, 21, 22] In patients without hypertension, the absence may be linked to tumor enzymatic profiles, notably the expression of catechol-O-methyltransferase, which inactivates catecholamines into metanephrines and may mask classic symptoms. [23]

Diabetes was observed in 30.8% of patients, aligning with the known effects of catecholamines on glucose metabolism, including insulin resistance, suppression of insulin secretion, and stimulation of glucagon production. [16, 24]

The average tumor size in our cohort (63.47 ± 30.44 mm) exceeded that reported in several series, including those by Legmann (45 mm) and Noblet-Dick (50 mm), but remained similar to values reported in other cohorts, such as Zouihri et al. (68 mm) and Lu et al. (50.1 ± 20.6 mm). [8, 18, 19, 21]

Spontaneous density (SD), though underreported in the literature, averaged 39.76 ± 17.62 HU in our series, with no cases below 10 HU, reinforcing current diagnostic thresholds and mirroring results from Lu et al. [16, 17, 21]

A statistically significant positive correlation was identified between tumor size and metanephrine levels ($R = 0.19$; $p < 0.001$), corroborating the findings of Aggarwal et al. ($R = 0.52$; $p < 0.0001$) [9], and supporting the hypothesis that larger tumors may contribute to higher catecholaminergic output.

Our data also confirmed key distinctions between sporadic and hereditary forms. Hereditary pheochromocytomas were diagnosed at a significantly younger age (34 ± 13.31 years vs. 41 ± 16.38 years; $p = 0.020$) and were more frequently bilateral (57.14% vs. 4.2%; $p = 0.040$). No significant differences were found concerning hypertension, Ménard's triad, or tumor size. These results align with those of El Amel et al. in Morocco, who also observed earlier diagnosis and bilaterality in hereditary forms, reinforcing the importance of genetic screening in selected patients. [25]

Excluding genetically screened cases, 64.28% of our pheochromocytomas were discovered incidentally, versus 35.7% diagnosed after clinical symptoms. These findings echo those of Aggarwal et al. (69% incidentalomas vs. 28% symptomatic). [9]

Patients with incidentalomas were significantly older (49.5 vs. 31 years; p = 0.040), similar to trends reported by Aggarwal (62 vs. 42 years) and Hernandez (56.4 vs. 32.6 years). [9, 20] However, unlike Aggarwal, who reported smaller tumor sizes in incidentalomas (42 mm vs. 60 mm) and lower hormone levels, we found significantly larger tumors in this group (65.7 mm vs. 50.5 mm), with no significant difference in catecholamine levels. These results are more in line with those of Hernandez et al, who found no major difference in tumor size or hormonal activity between groups. [20]

Regarding outcomes, our study demonstrated blood pressure normalization in 60% of hypertensive patients and improvement in glycemic control in 46.6% of diabetic cases, comparable to the outcomes reported by Zouihri et al. (BP normalization: 63.15%, glycemic control: 54.5%) and Hernandez et al. (BP normalization: 60%). [18, 20]

Despite its strengths, this study is limited by its retrospective design, which carries inherent challenges such as incomplete data and missing records. Furthermore, the relatively limited availability of genetic testing reduced our capacity to fully characterize hereditary forms and their prognostic implications.

6. Conclusion

Our study underscores the high prevalence of pheochromocytoma diagnoses made incidentally, particularly in the context of adrenal incidentalomas. Cardiovascular complications remain common and can be severe, reinforcing the need for early detection and coordinated multidisciplinary care. While Ménard's triad was incomplete in nearly half of the cases, it remains an important clinical clue and warrants careful attention. These findings highlight the need to raise awareness among healthcare providers about this rare but potentially life-threatening tumor, particularly when diagnosis is delayed.

Human Ethics and Consent to Participate declarations:

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. The research protocol was approved by the Ethics Committee of Bologhine Hospital (Algiers, Algeria). Given the retrospective nature of the study and the use of anonymized data, the requirement for informed consent was waived by the ethics committee.

Declarations

Postal adress

Endocrinology departement Bologhine, hospital Algiers ,Algeria

Consent to Participate:

Not applicable. The Ethics Committee of Bologhine Hospital waived the requirement for individual informed consent due to the retrospective design and full anonymization of the data used.

Author Contribution

W.D :collected the data, performed the analysis.wrote the main manuscript textM.M :conceived and designed the study,Reviewed the manuscriptAll authors reviewed the manuscript

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

- Human Ethics and Consent to Participate declarations: not applicable

- Clinical trial number: not applicable.

- Ethical Approval and consent to participate : Not applicable

-Consent to Publication : Not applicable

-Data Availability statement : yes

-Conflict of interest : no conflict

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-Author information (optional).

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Figures

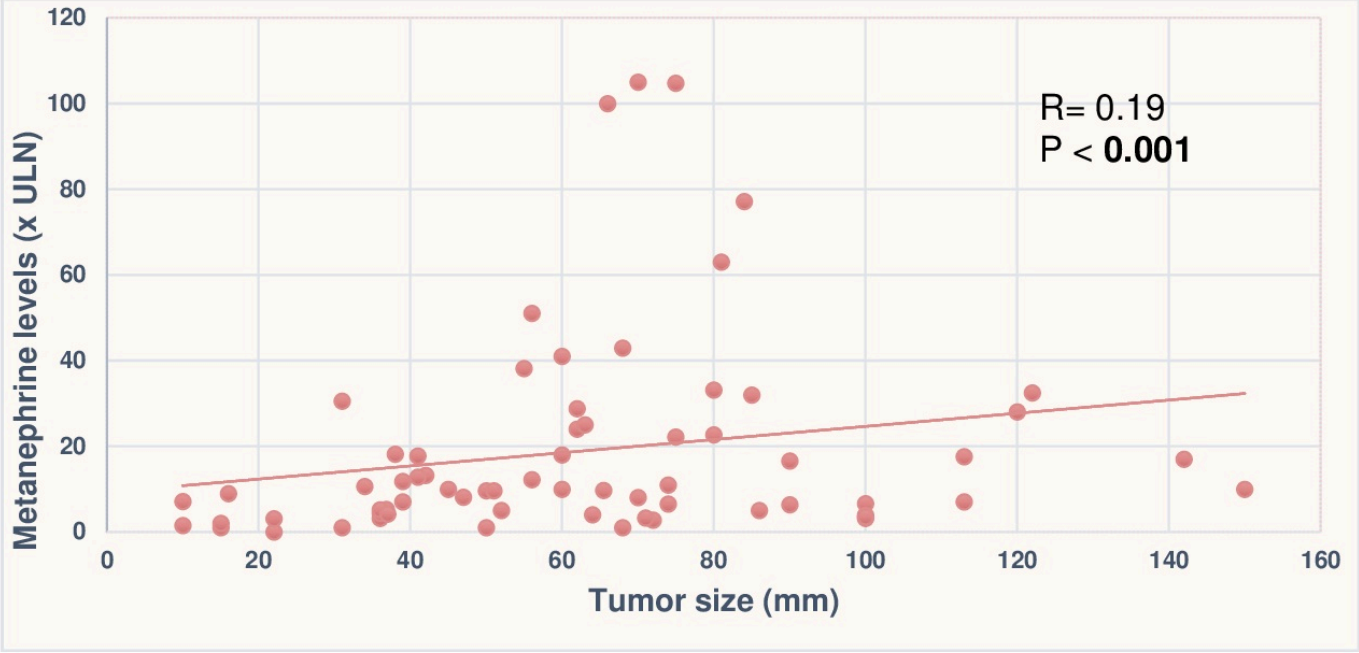


Figure 1: Correlation between tumor size and metanephrine levels.

Figure 1

See image above for figure legend

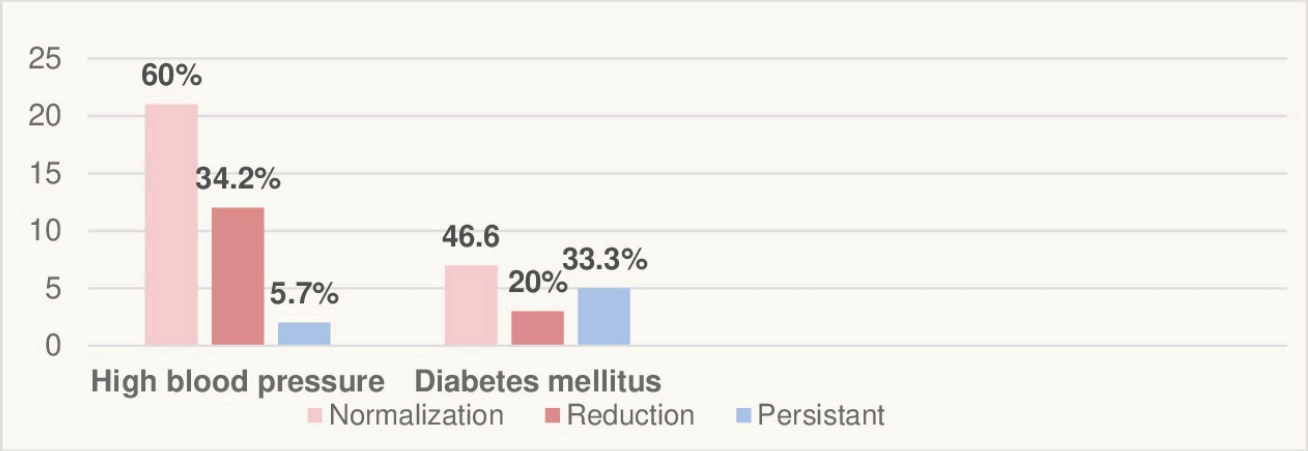


Figure 2: Postoperative evolution in our cohort.

Figure 2

See image above for figure legend