



Diabetes Update

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Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you **"DIABETES UPDATE"** which contains latest and interesting news in the field of Diabetes and Endocrinology.

- Skeletal muscle mass and its variation are associated with the development of diabetes
- A study on Prognostic nutritional index level and diabetes state are related to the prognosis of coronary artery disease.
- A study on association of C-peptid and renal progression in patients with type 2 diabetes
- A Case Report and Literature Analysis of a Cortisol-Secreting Adrenal Adenoma Associated With a Micro-Pheochromocytoma

Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Limited

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Skeletal muscle mass and its variation are associated with the development of diabetes

Type 2 diabetes mellitus (T2DM) has become a major global public health and research priority due to its ubiquity as a chronic metabolic condition. Several variables that result in insulin resistance and β -cell dysfunction lead to T2DM. A degenerative condition called sarcopenia increases the risk of falls, fragility, fractures, disability, hospitalisation, and mortality. It also causes reduced muscle strength or poor physical performance.¹ The purpose of this study was to investigate if changes in muscle mass are related to a higher risk of developing diabetes in a population located in a community.²

In this study, 1275 participants were enrolled who did not have diabetes at baseline. Participants completed the risk factors questionnaire and had their body composition measured at the baseline and follow-up exams. The definition of muscle mass index is the percentage of skeletal muscle mass as determined by an automatic bioelectric analyzer.

A median follow-up of 2.1 years later, 142 people (11.1%) had diabetes. Among participants with poor glucose control but not in those with normal glucose tolerance, there was an inverse relationship between baseline skeletal muscle mass index and the risk of diabetes. The risk of getting diabetes was associated with multivariate-adjusted hazard ratios of 0.85 (95% CI: 0.74-0.98) and 1.15 (95% CI: 0.98-1.34), respectively. Additionally, Cox regression analysis showed that in both participants with normal glucose tolerance and those with impaired glucose regulation, a two-year change in skeletal muscle mass was inversely associated with the incidence of diabetes (HR: 0.76, 95% CI: 0.65-0.89; HR: 0.81, 95% CI: 0.71-0.91).

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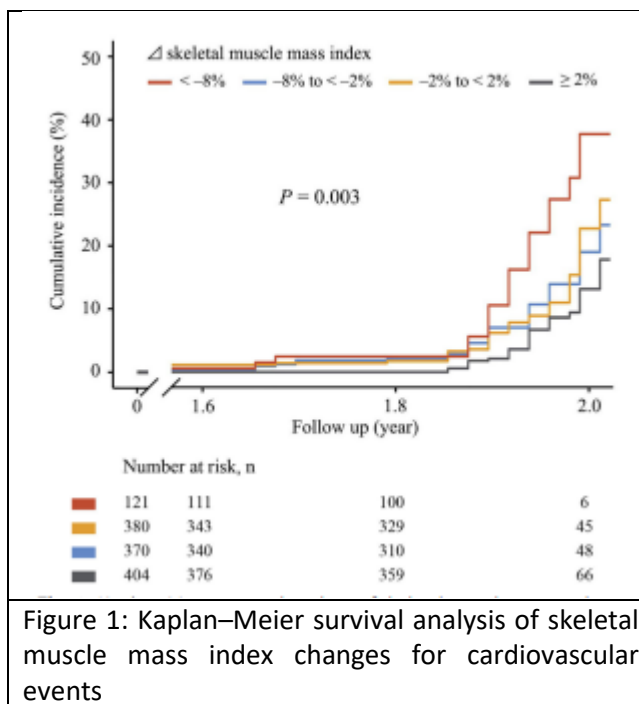


Figure 1: Kaplan–Meier survival analysis of skeletal muscle mass index changes for cardiovascular events

These results highlight the significance of early muscle mass loss identification and management in the prevention of diabetes. Low muscle mass is not the only factor that raises the risk of diabetes; growing muscle mass loss is also a risk factor.² Older skeletal muscle with reduced oxidative capacity was linked to altered mitochondrial biogenesis, which may be hampered by age-dependent accumulations of point mutations in human mitochondrial DNA (mt) as well as pro-inflammatory processes, according to prior research.³ Insulin resistance is linked to both chronic low-grade inflammation and mitochondrial dysfunction. Skeletal muscle insulin resistance is thought to be the beginning or basic problem that is obvious decades before -cell failure and overt hyperglycemia develops, despite the fact that -cell failure is the sine qua non for the development of type 2 diabetes.⁴

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This study showed that the incidence of diabetes was not only associated with low muscle mass at baseline but also with changes in skeletal muscle mass during a two-year period. Not only does having low muscle mass increase the chance of developing diabetes, but also losing muscle mass.

References:

1. Lu L, Liu B, Ma Y. Association of Different Obesity Phenotypes with Sarcopenia in Han Chinese Middle-Aged and Elderly with Type 2 Diabetes Individuals. *Diabetes Metab Syndr Obes.* 2023 Mar 21;16:841-848.
2. Xu Y, Hu T, Shen Y, Wang Y, Bao Y, Ma X. Association of skeletal muscle mass and its change with diabetes occurrence: a population-based cohort study. *Diabetol Metab Syndr.* 2023 Mar 22;15(1):53.
3. Li Y, Ma Q, Li P, Wang J, Wang M, Fan Y, et al. Proteomics reveals different pathological processes of adipose tissue, liver, and skeletal muscle under insulin resistance. *J Cell Physiol.* 2020;235(10):6441–61.
4. da Silva Rosa SC, Nayak N, Caymo AM, Gordon JW. Mechanisms of muscle insulin resistance and the cross-talk with liver and adipose tissue. *Physiol Rep.* 2020;8(19):e14607.

A study on Prognostic nutritional index level and diabetes state are related to the prognosis of coronary artery disease.

Globally, the prevalence of T2DM has been rising (463 million in 2019 to 700 million by 2045 in aged 20–79 yrs). In disease management and patient care, measuring well-being or health-related quality of life (HRQoL) has been a crucial topic.¹ In patients with diabetes or coronary artery disease, malnutrition and inflammation are linked to poor clinical results (CAD). A comprehensive and straightforward indicator reflecting nutritional state and immunological status is the prognostic nutritional index (PNI). Uncertainty

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exists regarding the impact of nutritional-immunological status and diabetic status on the prognosis of coronary artery disease (CAD).²

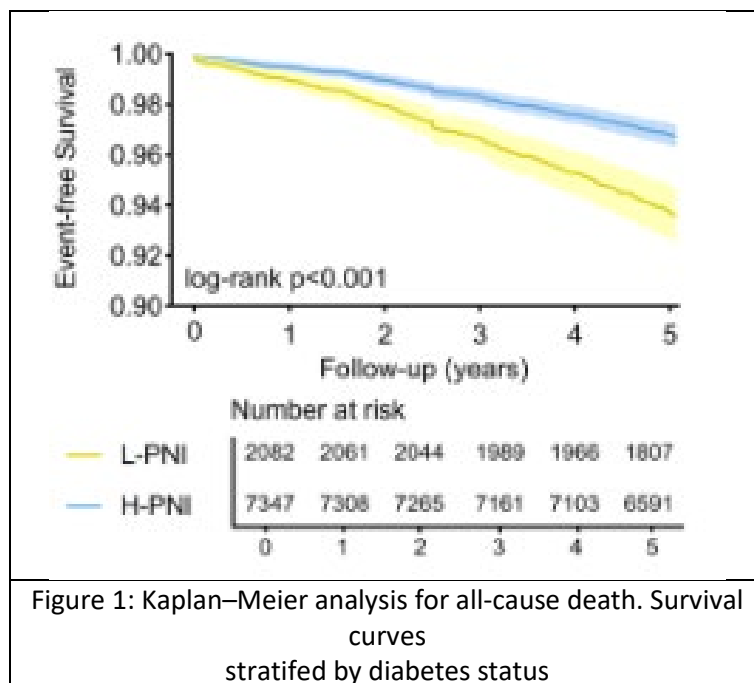
The statistically ideal cut-off value of 48.49 was used to group 9429 consecutive CAD patients undergoing percutaneous coronary intervention into two groups: those with diabetes (DM) and those without (non-DM) as well as those with high or low preprocedural Prognostic nutritional index (PNI) levels.

The study Compared with the non-DM/ H-PNI group, the DM/L-PNI group yielded the highest risk of all-cause death (adjusted hazard ratio: 2.65, 95% confidence interval: 1.97-3.56, $p < 0.001$), followed by the non-DM/L-PNI group (adjusted hazard ratio: 1.44, 95% confidence interval: 1.05-1.98, $p = 0.026$), while DM/H-PNI was not associated with the risk of all-cause death. L-PNI had a significantly worse effect on all-cause mortality in diabetes patients compared to non-diabetic patients (p for interaction = 0.037). (Figure 1) The Global Registry of Acute Coronary Events (GRACE) risk score for predicting all-cause death in patients with acute coronary syndrome, notably in those with diabetes, was significantly enhanced by preprocedural PNI categorization.

The joint impact and interaction of PNI level and diabetes status on 5-year outcomes following PCI in CAD patients are first evaluated in this study. The study discovered that patients with diabetes and L-PNI had the highest risk of death from all causes; the adverse effects of L-PNI on death from all causes were noticeably more pronounced in diabetic patients than in nondiabetic patients; and the addition of the preprocedural PNI category significantly improved model performance and the clinical net benefit of the GRACE risk score for predicting death from all causes, especially in diabetic patients. The predictive significance of nutritional-immunological condition and its association with diabetic status for CAD patients is highlighted by these findings.

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This study provides the first assessment of the interaction and joint effects of PNI level and diabetes status on 5-year outcomes following PCI in CAD patients. The study discovered that patients with diabetes and L-PNI had the highest risk of death from all causes; the adverse effects of L-PNI on death from all causes were noticeably more pronounced in diabetic patients than in nondiabetic patients; and the addition of the preprocedural PNI category significantly improved model performance and the clinical net benefit of the GRACE risk score for predicting death from all causes, especially in diabetic patients. The predictive significance of nutritional-immunological condition and its association with diabetic status for CAD patients is highlighted by these findings.³

Patients with CAD who also had diabetes and L-PNI had the worst outcome. Diabetes amplifies L-harmful PNI's effects on all-cause mortality. In CAD patients, poor nutritional-immunological state

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raises the risk of death from all causes more than diabetes does. Preprocedural PNI can be a prognostic indicator for CAD patients, particularly those with diabetes, and can be used to assess nutritional and infectious risk.

Reference:

1. Park S, Jung S, Yoon H. The role of nutritional status in the relationship between diabetes and health-related quality of life. *Nutr Res Pract.* 2022 Aug;16(4):505-516.
2. Li T, Yuan D, Wang P, Zeng G, Jia S, Zhang C, Zhu P, Song Y, Tang X, Gao R, Xu B, Yuan J. Association of prognostic nutritional index level and diabetes status with the prognosis of coronary artery disease: a cohort study. *Diabetol Metab Syndr.* 2023 Mar 25;15(1):58.
3. Rajamanickam A, Munisankar S, Dolla CK, Thiruvengadam K, Babu S. Impact of malnutrition on systemic immune and metabolic profiles in type 2 diabetes. *BMC Endocr Disord.* 2020;20(1):168.

A study on association of C-peptid and renal progression in patients with type 2 diabetes

Chronic kidney disease (CKD) and end-stage renal disease (ESRD) are now mostly caused by diabetic kidney disease (DKD), a major microvascular consequence of diabetes¹. The primary measures to counteract the development of negative clinical consequences of diabetes mellitus are early detection of DKD and carrying out the most efficient tailored intervention (DM). In medicine, 1 C-peptide, a peptide of 31 amino acids that is released into the blood by pancreatic β -cells in the same molar ratio as insulin, is typically used to monitor β -cell function. Thus, this study intends to evaluate the link between C-peptide and advancement of renal function in patients with type 2 diabetic mellitus (T2DM).²

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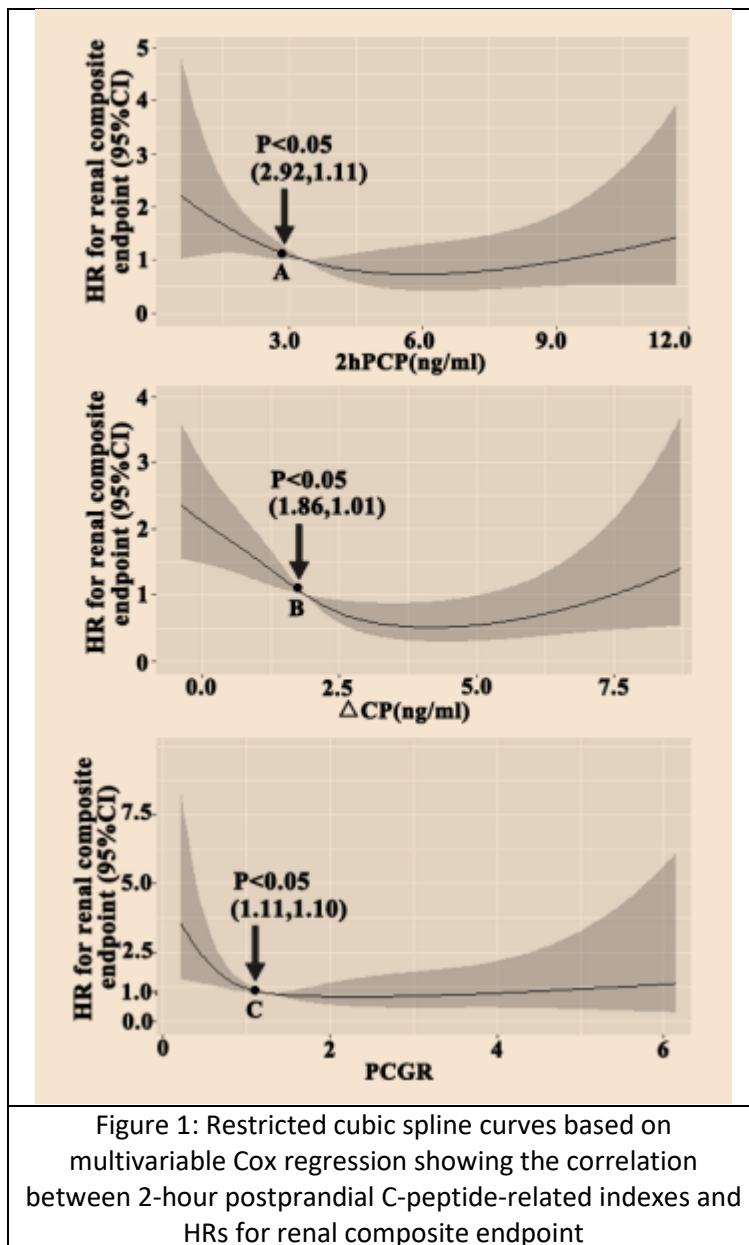
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Clinical information from 854 T2DM patients was gathered retrospectively by the researchers over a median follow-up of 5 years. A quick reduction in kidney function, an annual decline in estimated glomerular filtration rate (eGFR), and a renal composite endpoint were all renal events. After stratification by risk factors, a subgroup analysis was carried out to examine the impact of C-peptide on renal events using a linear mixed-effects model and Cox regression analysis.

The yearly eGFR drop was less in the highest-level C-peptide group compared to the lowest-level group ($p < 0.05$). Increased levels of the 2 h postprandial C-peptide (2hPCP) (adjusted HR 0.53; 95%CI 0.31 to 0.92), the difference between the 2 h postprandial and fasting C-peptide (CP) (adjusted HR 0.39; 95%CI 0.22 to 0.69), and the 2 h postprandial C-peptide-to-glucose ratio (PCGR) (adjusted HR 0. Among T2DM patients with male sex, age 65, illness duration 10 years, and a glycosylated haemoglobin level 7%, 2hPCP 2.92 ng/mL, CP 1.86 ng/mL, and PCGR 1.11 significantly elevated the probability of advancement in kidney function (adjusted HRs 0.50, $p < 0.05$). (Figure 1)

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The number of individuals with ESRD brought on by DM is still rising, and current clinical treatments can only partially stop the decline of renal function in T2DM.² small cross-sectional studies in China demonstrated that low- level C-peptide was an independent risk factor for proteinuria in T2DM patients. 3 Relevant studies have revealed that male sex, age, illness course, race, family history, obesity, high-protein diet, hyperglycemia, hypertension, etc. are risk factors for DKD. The results were inconclusive with regard to age and diabetes duration, which may have been caused by the reduced percentage of elderly patients or patients with advanced disease in the population in the trial with a high level of 2hPCP.⁴

Increased levels of 2hPCP, CP, and PCGR, notably in the previously described demographic of diabetics, may shield T2DM patients from renal deterioration.

Reference:

1. .Xin S, Zhao X, Ding J, Zhang X. Association between hemoglobin glycation index and diabetic kidney disease in type 2 diabetes mellitus in China: A cross-sectional inpatient study. *Front Endocrinol (Lausanne)*. 2023 Mar 8;14:1108061.
2. Yang Q, Liu Y, Peng J, Pan J, Chen L, Cui J, Yi B. High levels of serum C-peptide are associated with a decreased risk for incident renal progression in patients with type 2 diabetes: a retrospective cohort study. *BMJ Open Diabetes Res Care*. 2023 Mar;11(2):e003201.
3. Zhou Y, Chen K, Du X, et al. Risk factors for albuminuria in normotensive older adults with type 2 diabetes mellitus and normal renal function: a cross-sectional study. *Diabetes Ther* 2021;12:697–705.
4. López-Heydeck SM, Robles-Navarro JB, Montenegro-Morales LP, et al. Factores de riesgo y de estilo de vida asociados a enfermedad renal crónica [Risk and lifestyle factors associated to chronic kidney disease]. *Rev Med Inst Mex Seguro Soc* 2020;58:305–16.

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A Case Report and Literature Analysis of a Cortisol-Secreting Adrenal Adenoma Associated With a Micro-Pheochromocytoma

Long-term exposure to excessive cortisol levels in the bloodstream results in Cushing syndrome. Iatrogenic corticosteroid use is the most frequent cause of cushingoid characteristics, although several herbal remedies can also raise circulating corticosteroid levels, which can result in Cushing syndrome. The terms Cushing syndrome and hypercortisolism are interchangeable.¹ Pheochromocytomas (PCCs), on the other hand, are tumours that develop from chromaffin cells of the adrenal medulla, which frequently produce catecholamines (epinephrine, norepinephrine, and dopamine). Endocrine hypertension is linked to both PCCs and Cushing's syndrome. The instance of a tiny PCC that was unintentionally discovered after a laparoscopic adrenalectomy for a cortisol-secreting adrenal adenoma is shown in this article. By using immunohistochemistry analysis, the study assessed catecholamine production.²

Case Presentation:

A left adrenal tumour that increased in size from 1 to 2 cm in a year was referred to our hospital for further assessment in a 53-year-old lady. Amlodipine and pravastatin were administered for her seven years of hypertension and dyslipidemia, respectively. A left adrenalectomy was carried out laparoscopically. At completion of the pathological analysis, a 2624mm adrenocortical adenoma was found. A micro-PCC measuring 3 2 mm was also unintentionally discovered in the ipsilateral adrenal gland next to the cortisol-secreting adrenal adenoma. By using immunohistochemical techniques, all catecholamine biosynthesis enzymes, including tyrosine hydroxylase, aromatic l-amino acid decarboxylase, dopamine -hydroxylase, and phenyl ethanolamine N-methyltransferase, were found in this micro-

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PCC. (Figure 2) The PCC expressed catecholamine synthesis enzymes despite the fact that catecholamine levels were not biochemically raised.

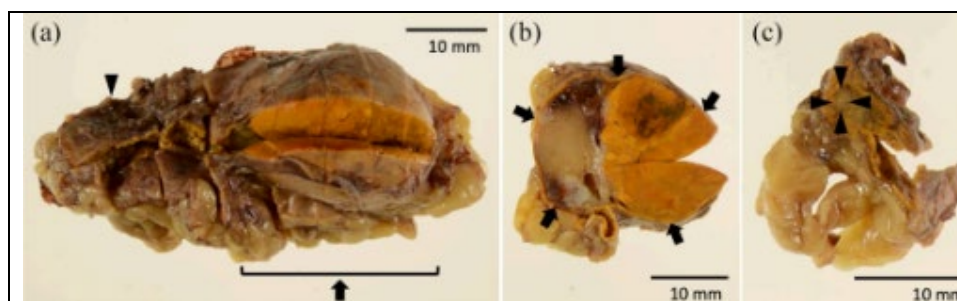


Fig 1: (a) Positional relationship of the adrenocortical adenoma (arrow) and micro-pheochromocytoma (arrowhead). Sectional views of (b) the adrenocortical adenoma and (c) the micro-pheochromocytoma

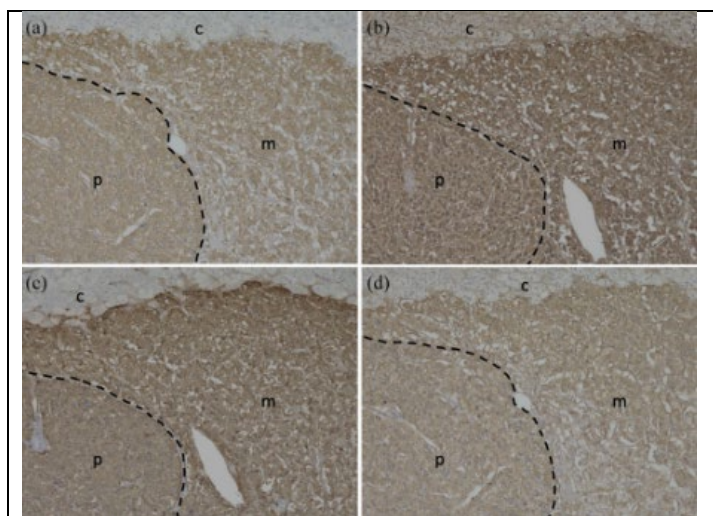


Fig 2: 3. Immunohistochemical staining of the micro-pheochromocytoma with (a) tyrosine hydroxylase (TH), (b) aromatic L-amino acid decarboxylase (AADC), (c) dopamine β -hydroxylase (DBH), and (d) phenylethanolamine N-methyltransferase (PNMT) antibodies

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After a laparoscopic adrenalectomy to remove a cortisol-secreting adrenal adenoma, a micro-PCC was unintentionally found. Since micro-PCC was too small to be seen by imaging tests and could not be detected by endocrinological laboratory testing, the study was unable to predict its presence. After surgery, the levels of urinary fractionated metanephrines did not change, hence the investigation was unable to discover excess catecholamine productions in the past. The pre-biochemical phase of the micro-PCC was thought to be present.² In the immediate surroundings, there is interaction between the medulla and the adrenal cortex.³ In this instance, the adrenocortical adenoma's secretion of glucocorticoids may have aided in the development of micro-PCC in the medulla. The adrenocortical adenoma may have been activated and glucocorticoid synthesis increased as a result of the extra catecholamines that micro-PCC generated. Hence, elevated glucocorticoids may have assisted in the development of lipomatous alterations. The only way this study can conclude that this micro-pheochromocytoma produced catecholamines is because immunohistochemistry markers for catecholamine biosynthesis are positive.³

Due to the rarity of silent micro-PCCs in clinical settings, it is uncertain if they create catecholamines during the pre-biochemical phase. This is the first immunohistochemical report of a micro-PCC that was producing catecholamines prior to the biochemical phase.

References:

1. Chaudhry HS, Singh G. Cushing Syndrome. [Updated 2023 Jan 1]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK470218/>
2. Sakai K, Asano M, Hamaguchi M, Taniguchi H, Ukimura O, Fukui M. A Cortisol-Secreting Adrenal Adenoma Combined With a Micro-Pheochromocytoma: Case Report and Literature Review. Clin Med Insights Endocrinol Diabetes. 2023 Jan 16;16:11795514221148556.



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3. Constantinescu G, Langton K, Conrad C, et al. Glucocorticoid excess in patients with pheochromocytoma compared with paraganglioma and other forms of hypertension. J Clin Endocrinol Metab. 2020;105:e3374-e3383.

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