Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Preoperative and Postoperative Serum Profiles of Cathelicidin/LL-37 and Associated Molecular Markers in Papillary Thyroid Cancer

Nurcan Umur

nurcan.umur@cbu.edu.tr

Manisa Celal Bayar University

Funda Kosova

Manisa Celal Bayar University

Bahadır Çetin

Ankara Oncology Training and Research Hospital, Health Sciences University

Research Article

Keywords: thyroid cancer, cathelicidin/LL-37, vitamin D receptor, neutrophil elastase, elafin, tumor microenvironment

Posted Date: November 26th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11783435/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

This exploratory study evaluated circulating cathelicidin/LL-37, vitamin D receptor (VDR), neutrophil elastase (NE), and elafin levels in patients with thyroid cancer and assessed early postoperative changes. The study included 25 patients with papillary thyroid carcinoma and 20 healthy controls. Paired blood samples were collected immediately before surgery and on postoperative day 20. Serum concentrations were measured using enzyme-linked immunosorbent assays. Independent-group comparisons were performed using the Mann–Whitney U test, and paired measurements were analyzed using the Wilcoxon signed-rank test. LL-37 and VDR levels were significantly higher, whereas NE levels were significantly lower, in patients at both time points than in controls. Elafin levels did not differ significantly between controls and preoperative measurements but decreased significantly after surgery. No significant preoperative–postoperative changes were observed in LL-37, VDR, or NE. These findings characterize circulating profiles of molecules associated with innate immunity, vitamin D signaling, and protease–antiprotease regulation in thyroid cancer. Their combined assessment in paired samples provides preliminary data for further investigation. Studies incorporating tissue expression, enzymatic activity, and clinical outcomes are needed to clarify the biological significance and potential biomarker value of these findings.

1. Introduction

Thyroid cancer is the most common malignancy of the endocrine system and exhibits considerable heterogeneity in its clinical behavior and response to treatment. Although most differentiated thyroid carcinomas follow an indolent course and have a favorable prognosis, a subset of tumors demonstrates aggressive progression, local invasion, metastatic spread, and resistance to conventional therapies. The incidence of thyroid cancer has increased substantially in recent decades. While improved imaging and diagnostic practices account for a considerable proportion of this increase, epidemiological evidence suggests that additional biological, environmental, and lifestyle-related factors may also contribute [1, 2].

In addition to genetic and epigenetic alterations, thyroid cancer development and progression are increasingly recognized as dynamic processes influenced by the tumor microenvironment. Interactions among tumor cells, immune cells, inflammatory mediators, stromal components, and extracellular matrix-remodeling enzymes may affect tumor growth, invasion, metastatic potential, and therapeutic response [3, 4]. Antimicrobial peptides have consequently attracted attention as potential mediators at the interface between innate immunity, inflammation, and cancer biology.

Cathelicidin LL-37 is the only member of the cathelicidin antimicrobial peptide family identified in humans. It is generated from the precursor protein human cationic antimicrobial protein 18 (hCAP18), encoded by the CAMP gene, and is expressed by neutrophils, macrophages, epithelial cells, and other cell types. In addition to its antimicrobial activity, LL-37 regulates inflammatory responses, immune-cell recruitment, angiogenesis, cell proliferation, migration, and apoptosis [5, 6]. Its effects in cancer appear to be highly context-dependent. Increased LL-37 levels have been associated with tumor growth and

progression in several malignancies, whereas antitumor effects have been reported in others. These apparently opposing actions are thought to depend on tumor type, peptide concentration, receptor expression, and the cellular and inflammatory characteristics of the tumor microenvironment [6, 7].

An important regulator of cathelicidin expression is the vitamin D signaling pathway. The biologically active form of vitamin D, 1,25-dihydroxyvitamin D_3, binds to the vitamin D receptor (VDR), a ligand-activated nuclear transcription factor involved in the regulation of cellular proliferation, differentiation, apoptosis, and immune responses. The CAMP gene is a direct transcriptional target of VDR, providing a mechanistic link between vitamin D signaling and cathelicidin expression [8]. Dysregulation of vitamin D/VDR signaling has been implicated in the development and progression of several malignancies. In papillary thyroid cancer, alterations in VDR expression have been associated with serum vitamin D status and clinicopathological indicators of disease aggressiveness. However, available findings remain heterogeneous, and the precise role of vitamin D/VDR signaling in thyroid carcinogenesis has not been fully established [9, 10].

Proteolytic regulation represents another important component of the inflammatory tumor microenvironment. Neutrophil elastase (NE), a serine protease primarily released by activated neutrophils, can degrade extracellular matrix proteins and modulate intracellular and extracellular signaling pathways. Depending on the biological context, NE may contribute to tumor-cell proliferation, invasion, intravasation, and metastatic progression [11, 12]. Nevertheless, neutrophil-derived proteases may also exhibit context-dependent antitumor activity, illustrating the complexity of protease function in cancer [13].

Elafin, also known as peptidase inhibitor 3 (PI3), is an endogenous inhibitor of neutrophil serine proteases, particularly NE and proteinase 3. By limiting excessive proteolysis, elafin contributes to the preservation of epithelial integrity and the regulation of inflammatory responses [14, 15]. Disturbance of the balance between NE and elafin may therefore promote tissue injury, extracellular matrix remodeling, and persistent inflammation. However, the biological significance of this protease–antiprotease balance varies among cancer types and remains insufficiently characterized in thyroid cancer.

Collectively, these observations suggest that vitamin D/VDR-regulated cathelicidin expression and the NE/elafin protease–antiprotease system may represent complementary components of the inflammatory and immune microenvironment. Although direct regulation of CAMP by VDR and inhibition of NE by elafin are well established, whether these systems interact in thyroid cancer has not yet been determined. Therefore, describing LL-37, VDR, NE, and elafin as components of a potentially interconnected molecular network is more appropriate than assuming the existence of a previously established unified pathway.

This study was designed as a preliminary, exploratory mapping study evaluating circulating cathelicidin/LL-37, VDR, NE, and elafin profiles in patients with thyroid cancer before and after surgery, in comparison with healthy controls. The aim was to characterize patterns in the serum levels of these proteins. These findings may contribute to a better under-standing of the inflammatory and immune

mechanisms associated with thyroid cancer and provide a basis for future studies evaluating their potential biomarker value.

2. Materials and methods

2.1 Study Design

This study was approved by the Health Sciences Ethics Committee of Manisa Celal Bayar University (Decision No: 20.478.486/2594, 4 September 2024). Institutional permission was also obtained from the University of Health Sciences Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital. The study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants before enrollment.

The study included 25 patients with papillary thyroid carcinoma (PTC) who presented to the General Surgery Clinic of Ankara Oncology Hospital and 20 control participants. Of the patients, 5 were male and 20 were female, with a mean age of 42.8 ± 13.2 years. Patients were euthyroid, with normal thyroid function tests and normal total cholesterol and triglyceride levels. Individuals with diabetes mellitus or hypertension, those receiving hormonal treatments such as oral contraceptives, thyroxine derivatives, or estrogen replacement therapy, and those taking medication for chronic diseases were excluded. None of the patients had palpable lymph nodes on physical examination or lymph nodes detected by ultrasonography. All patients underwent total thyroidectomy without lymph node dissection. The diagnosis was confirmed by postoperative histopathological examination. Radioactive iodine was administered 5–6 weeks after thyroidectomy. None of the patients received thyroid hormone postoperatively in preparation for radioactive iodine therapy. Patients attended a follow-up visit on postoperative day 20. Blood samples were collected from each patient immediately before surgery and on postoperative day 20, and once from each control participant. Thus, the preoperative and postoperative samples represented paired measurements obtained from the same patients. The control group consisted of 20 healthy volunteers with a mean age of 39 ± 2.5 years who had no known acute, chronic, systemic, or malignant disease.The collected blood samples were centrifuged at 4500 rpm to separate the serum. Serum samples were divided into aliquots and stored at − 80°C until biochemical analysis.

2.2. ELISA Analysis

Serum concentrations of cathelicidin/LL-37, NE, PI3 and VDR were measured using commercially available human specific enzyme linked immunosorbent assay (ELISA) kits (Elabscience Biotechnology Inc., Houston, TX, USA).

The following kits were used; Human LL-37 (Antibacterial Protein LL-37) ELISA Kit (Cat. No. E-EL-H2438), Human NE (Neutrophil Elastase) ELISA Kit (Cat. No. E-EL-H1946), Human PI3/Elafin (Peptidase Inhibitor 3) ELISA Kit (Cat. No. E-EL-H2447), and Human VDR (Vitamin D Receptor) ELISA Kit (Cat. No. E-EL-H2043).

All assays were performed according to the manufacturer's instructions. Standards and serum samples were added to the appropriate antibody-precoated microplate wells. Following the specified incubation and washing steps, enzymatic reactions were developed using the supplied substrate solutions. Optical density was measured at 450 nm using a microplate reader. Serum concentrations were calculated using the corresponding standard curves.

2.3. Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics, version 23.0 (IBM Corp., Armonk, NY, USA). Data were expressed as mean ± standard deviation (SD). The Mann–Whitney U test was used to compare healthy controls with patients with thyroid cancer at each sampling time point. Paired preoperative and postoperative measurements were compared using the Wilcoxon signed-rank test. A p-value of < 0.05 was considered statistically significant.

3. Results

3.1. ELISA Results of Serum Protein Levels

Serum levels of cathelicidin/LL-37, Elafin, VDR and NE were measured by ELISA in healthy controls and patients with thyroid cancer before and after surgery. The results are presented in Table 1 and Fig. 1. Serum cathelicidin/LL-37 levels were significantly higher in both the preoperative (18.8 ± 7.5 ng/mL) and postoperative groups (18.9 ± 7.9 ng/mL) than in the control group (14.8 ± 11.0 ng/mL; $p < 0.05$), whereas no significant difference was observed between the preoperative and postoperative measurements ($p > 0.05$). Similarly, serum VDR levels were significantly higher in both the preoperative (4.3 ± 3.8 ng/mL) and postoperative groups (3.3 ± 2.4 ng/mL) than in the control group (1.9 ± 1.7 ng/mL; $p < 0.05$), while the difference between the preoperative and postoperative measurements was not statistically significant ($p > 0.05$). Serum elafin levels did not differ significantly between the control (381.2 ± 246.6 ng/L) and preoperative groups (397.8 ± 175.8 ng/L; $p > 0.05$). However, postoperative elafin levels (298.9 ± 127.9 ng/L) were significantly lower than preoperative levels ($p < 0.05$). No significant difference was observed between the control and postoperative groups ($p > 0.05$). Serum NE levels were significantly lower in both the preoperative (165.1 ± 12.3 ng/L) and postoperative groups (157.7 ± 21.0 ng/L) than in the control group (174.8 ± 7.7 ng/L; $p < 0.05$). Although the lowest numerical NE level was observed postoperatively, the difference between the preoperative and postoperative measurements was not statistically significant ($p > 0.05$).

Table 1
Serum biomarker levels in healthy controls and patients with thyroid cancer before and after surgery.

Group	Cathelicidin/LL-37 (ng/mL)	Elafin (ng/L)	VDR (ng/mL)	NE (ng/L)
Healthy controls (n = 20)	14.8 ± 11.0	381.2 ± 246.6	1.9 ± 1.7	174.8 ± 7.7
Preoperative (n = 25)	18.8 ± 7.5*	397.8 ± 175.8	4.3 ± 3.8*	165.1 ± 12.3*
Postoperative (n = 25)	18.9 ± 7.9*	298.9 ± 127.9**	3.3 ± 2.4*	157.7 ± 21.0*

Data are presented as mean ± standard deviation (SD).

*p < 0.05 compared with the healthy control group.

**p < 0.05 compared with the preoperative measurement.

4. Discussion

Thyroid cancer is a heterogeneous malignancy in terms of clinical behavior and response to treatment. Although most differentiated thyroid cancers have a favorable clinical course, invasion, metastasis, recurrence, and treatment resistance may develop in some patients. Studies investigating the biology of thyroid cancer have also addressed the interactions among immune cells, stromal components, cytokines, and the extracellular matrix within the tumor microenvironment [3]. In this context, antimicrobial peptides, vitamin D-related regulatory molecules, and the protease–antiprotease system are among the subjects under investigation. Against this biological background, the present study was designed as a preliminary, exploratory profiling study to evaluate the circulating profiles of cathelicidin/LL-37, VDR, NE, and elafin.

In our study, preoperative and postoperative serum levels of cathelicidin/LL-37, VDR, NE, and elafin in patients with thyroid cancer were compared with those of healthy controls. Cathelicidin and VDR levels were significantly higher at both time points than in the control group, whereas NE levels were significantly lower. Elafin levels did not differ significantly between the control group and preoperative measurements but decreased significantly after surgery compared with preoperative levels. No significant differences were observed between preoperative and postoperative day 20 measurements for cathelicidin, VDR, or NE. These findings describe the serum profiles of the four investigated molecules in the same patient population and their changes during the early postoperative period.

In addition to its antimicrobial activity, LL-37 has functions associated with inflammation, immune cell migration, angiogenesis, cellular proliferation, and wound healing. Its effects in cancer biology vary depending on the tumor type and microenvironmental conditions. While antitumor effects have been reported in some studies, others have described effects associated with proliferation, cell migration, and

angiogenesis through signaling mechanisms involving FPR2, EGFR, and MAPK/ERK [6, 16]. These differences indicate that circulating LL-37 levels should not be interpreted unidirectionally as either promoting or suppressing tumor development.

In our study, serum cathelicidin/LL-37 levels were 14.8 ± 11.0 ng/mL in the control group, 18.8 ± 7.5 ng/mL preoperatively, and 18.9 ± 7.9 ng/mL postoperatively. Although levels in patients were significantly higher than those in controls at both time points, no significant difference was observed between preoperative and postoperative levels. Therefore, no significant reduction in cathelicidin/LL-37 levels was identified on postoperative day 20 in our study. This observation represents a finding related to the serum profile. A study investigating postoperative inflammatory changes in thyroid diseases reported that certain inflammatory cytokines, which were particularly elevated in patients with papillary thyroid cancer, decreased during the postoperative period [17]. A similar decrease in cathelicidin/LL-37 levels was not observed in our study. Measurements at different follow-up time points would be useful for a more detailed evaluation of the postoperative course of cathelicidin/LL-37. The biological properties of cathelicidin/LL-37 may also vary depending on its proteolytic processing and the resulting peptide fragments. A review reported that different cathelicidin/LL-37 derivatives may exhibit distinct antimicrobial, immunomodulatory, and proliferative effects [18]. In our study, serum concentrations of LL-37 were measured; however, these measurements do not provide direct evidence regarding its activity within the tumor microenvironment.

The vitamin D/VDR signaling system plays a role in regulating cellular differentiation, proliferation, apoptosis, and immune responses. Active vitamin D binds to VDR and regulates the transcription of target genes. The vitamin D response element located in the promoter region of the CAMP gene represents one of the established links between vitamin D/VDR signaling and cathelicidin expression [8, 19, 20]. This relationship provides a biological rationale for evaluating cathelicidin and VDR together in the same samples. However, simultaneous measurement of their circulating concentrations does not directly demonstrate the activity of this signaling pathway. Serum VDR levels were 1.9 ± 1.7 ng/mL in the control group, 4.3 ± 3.8 ng/mL preoperatively, and 3.3 ± 2.4 ng/mL postoperatively. Although both patient measurements were significantly higher than those of the control group, the difference between preoperative and postoperative values was not statistically significant. Therefore, the numerical decrease observed after surgery was not interpreted as a significant surgery-related change in VDR levels. VDR expression in papillary thyroid cancer tissue has been reported to be associated with clinicopathological characteristics [9]. Furthermore, a pan-cancer analysis identified associations between VDR expression and stromal and immune components of the tumor microenvironment, while experimental investigations involving papillary thyroid cancer reported that increased VDR expression may suppress cellular proliferation and migration [21]. These studies provide information regarding the functions of VDR at the tissue level. In our study, the finding that cathelicidin and VDR levels were higher than those of the control group at both time points was interpreted as a concurrently observed serum pattern; this finding does not establish a causal relationship between the two molecules.

NE is a serine protease released from the azurophilic granules of activated neutrophils. It is involved in processes such as extracellular matrix degradation, cytokine processing, regulation of inflammatory responses, and tissue remodeling. The effects of NE in cancer models have been reported to vary depending on the experimental conditions. While some studies have described effects associated with tumor invasion and proliferative signaling, other experimental models have demonstrated direct cytotoxic effects against tumor cells [11–13, 22]. In our study, serum NE levels were 174.8 ± 7.7 ng/L in the control group, 165.1 ± 12.3 ng/L preoperatively, and 157.7 ± 21.0 ng/L postoperatively. Levels at both patient time points were significantly lower than those in the control group. Although a lower mean value was observed after surgery, the difference between preoperative and postoperative measurements was not statistically significant. A study investigating the clinical relevance of circulating neutrophil elastase for disease monitoring and recurrence detection in differentiated thyroid cancer reported findings regarding its potential utility [23].

Elafin is an endogenous antiprotease encoded by the PI3 gene that inhibits neutrophil serine proteases, particularly NE. Its functions are associated with limiting protease-mediated tissue damage, regulating inflammatory responses, and maintaining epithelial integrity [14, 15]. The effects of elafin in cancer biology may also vary according to tumor type. While protective functions have been described in some studies, increased elafin expression has been associated with tumor behavior and immune cell infiltration in others [24]. In our study, serum elafin levels were 381.2 ± 246.6 ng/L in the control group, 397.8 ± 175.8 ng/L preoperatively, and 298.9 ± 127.9 ng/L postoperatively. No significant difference was observed between the control group and preoperative measurements, whereas postoperative levels were significantly lower than preoperative levels. Among the four molecules investigated, elafin was the only molecule that showed a significant change in the preoperative–postoperative comparison. Caruso et al. reported that elafin may contribute to the maintenance of normal growth control by inhibiting the mitogenic effects of NE [25]. This experimental finding supports the biological rationale for evaluating NE and elafin together.

It has also been reported that fragments generated through the proteolytic processing of LL-37 may exhibit biological properties distinct from those of the parent peptide [18]. This information provides a background for investigating the relationships between antimicrobial peptides and the protease system. However, the present study did not evaluate LL-37 degradation, its processing by NE, or the effects of elafin on this process. Therefore, the combined investigation of the four molecules was considered a joint characterization of their circulating profiles within the same study population rather than a demonstration of a shared molecular pathway.

One strength of this study is that preoperative and postoperative samples were obtained from the same patients and that cathelicidin/LL-37, VDR, NE, and elafin were evaluated in the same set of samples. The paired design reduced the influence of interindividual variability on preoperative–postoperative comparisons, allowing within-patient changes to be examined. The combined evaluation of the four molecules also provides comparative serum profiles beyond measurements focusing on a single molecule.

The single-center design and sample size of this study warrant confirmation of the findings in larger patient populations. Because the evaluations were based on serum measurements, the results should be interpreted in the context of circulating protein levels. Although paired samples obtained from the same patients enabled the assessment of the early postoperative period, studies incorporating additional follow-up time points and tissue analyses may contribute to a better understanding of the biological significance of the observed profiles.

5. Conclusions

This exploratory study characterizes the preoperative and postoperative serum profiles of cathelicidin/LL-37, VDR, NE, and elafin in patients with thyroid cancer. Cathelicidin and VDR levels were higher than those in the control group at both time points, whereas NE levels were lower, and a significant postoperative reduction was observed in elafin levels. The combined and paired evaluation of these four molecules in the same patient population provides preliminary data on their circulating profiles and establishes a basis for further investigations into their biological relationships.

Declarations

Author Contributions: N.U., F.K.: study design, data analysis, and manuscript preparation; B.Ç.: study design, manuscript preparation.

Funding: This study was supported by the Scientific Research Coordination Unit of Manisa Celal Bayar University (No: 2024-115).

Institutional Review Board Statement: This study was approved by Manisa Celal Bayar University Health Sciences Ethics Committee (Decision No: 20.478.486/2594, 4 September 2024).

Informed Consent Statement: For human blood samples, informed consent was obtained from all participants regarding their participation in the study or the use of their samples.

Data Availability Statement: The original contributions presented in this study are included in the article. Further inquiries can be directed to the corresponding author.

Acknowledgments: We would like to thank the Scientific Research Coordination Unit of Manisa Celal Bayar University for supporting this study.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Sanabria A, Kowalski LP, Shah JP, Nixon IJ, Angelos P, Williams MD, et al. Growing incidence of thyroid carcinoma in recent years: Factors underlying overdiagnosis. Head Neck. 2018;40(4):855–66. 10.1002/hed.25029.

2. La Vecchia C, Malvezzi M, Bosetti C, Garavello W, Bertuccio P, Levi F, et al. Thyroid cancer mortality and incidence: A global overview. Int J Cancer. 2015;136(9):2187–95. 10.1002/ijc.29251.
3. MacDonald L, Jenkins J, Purvis G, Lee J, Franco AT. The thyroid tumor microenvironment: Potential targets for therapeutic intervention and prognostication. Horm Cancer. 2020;11(5–6):205–17. 10.1007/s12672-020-00390-6.
4. Menicali E, Guzzetti M, Morelli S, Moretti S, Puxeddu E. Immune landscape of thyroid cancers: New insights. Front Endocrinol (Lausanne). 2021;11:637826. 10.3389/fendo.2020.637826.
5. Wu WKK, Wang G, Coffelt SB, Betancourt AM, Lee CW, Fan D, et al. Emerging roles of the host defense peptide LL-37 in human cancer and its potential therapeutic applications. Int J Cancer. 2010;127(8):1741–7. 10.1002/ijc.25489.
6. Piktel E, Niemirowicz K, Wnorowska U, Wątek M, Wollny T, Głuszek K, et al. The role of cathelicidin LL-37 in cancer development. Arch Immunol Ther Exp (Warsz). 2016;64(1):33–46. 10.1007/s00005-015-0359-5.
7. Kuroda K, Okumura K, Isogai H, Isogai E. The human cathelicidin antimicrobial peptide LL-37 and mimics are potential anticancer drugs. Front Oncol. 2015;5:144. 10.3389/fonc.2015.00144.
8. Gombart AF, Borregaard N, Koeffler HP. Human cathelicidin antimicrobial peptide (CAMP) gene is a direct target of the vitamin D receptor and is strongly upregulated in myeloid cells by 1,25-dihydroxyvitamin D_3. FASEB J. 2005;19(9):1067–77. 10.1096/fj.04-3284com.
9. Kim MJ, Kim D, Koo JS, Lee JH, Nam KH. Vitamin D receptor expression and its clinical significance in papillary thyroid cancer. Technol Cancer Res Treat. 2022;21:15330338221089933. 10.1177/15330338221089933.
10. Maciejewski A, Lacka K. Vitamin D-related genes and thyroid cancer—A systematic review. Int J Mol Sci. 2022;23(21):13661. 10.3390/ijms232113661.
11. Lerman I, Hammes SR. Neutrophil elastase in the tumor microenvironment. Steroids. 2018;133:96–101. 10.1016/j.steroids.2017.11.006.
12. Deryugina E, Carré A, Ardi V, Muramatsu T, Schmidt J, Pham C, Quigley JP. Neutrophil elastase facilitates tumor cell intravasation and early metastatic events. iScience. 2020;23(12):101799. 10.1016/j.isci.2020.101799.
13. Cui C, Chakraborty K, Tang XA, Zhou G, Schoenfelt KQ, Becker KM, et al. Neutrophil elastase selectively kills cancer cells and attenuates tumorigenesis. Cell. 2021;184(12):3163–e317721. 10.1016/j.cell.2021.04.016.
14. Guyot N, Zani ML, Maurel MC, Dallet-Choisy S, Moreau T. Elafin and its precursor trappin-2 still inhibit neutrophil serine proteinases when they are covalently bound to extracellular matrix proteins by tissue transglutaminase. Biochemistry. 2005;44(47):15610–8. 10.1021/bi051418i.
15. Deraison C, Bonnart C, Langella P, Roget K, Vergnolle N. Elafin and its precursor trappin-2: What is their therapeutic potential for intestinal diseases? Br J Pharmacol. 2023;180(2):144–60. 10.1111/bph.15985.

16. Lu F, Zhu Y, Zhang G, Liu Z. Repurposing human antibacterial peptide LL-37 for cancer treatment: A review. Front Pharmacol. 2022;13:944147. 10.3389/fphar.2022.944147.
17. Li H, Jin X, Zhang M, Wang X, Wang H. Differential expression of cytokines and vitamin D in benign and malignant thyroid diseases. Sci Rep. 2025;15:23493. 10.1038/s41598-025-06882-1.
18. Voronko OE, Khotina VA, Kashirskikh DA, Lee AA, Gasanov VAO. Antimicrobial peptides of the cathelicidin family: Focus on LL-37 and its modifications. Int J Mol Sci. 2025;26(16):8103. 10.3390/ijms26168103.
19. Chung C, Silwal P, Kim I, Modlin RL, Jo EK. Vitamin D–cathelicidin axis: At the crossroads between protective immunity and pathological inflammation during infection. Immune Netw. 2020;20(2):e12. 10.4110/in.2020.20.e12.
20. Wang TT, Nestel FP, Bourdeau V, Nagai Y, Wang Q, Liao J, et al. Cutting edge: 1,25-Dihydroxyvitamin D_3 is a direct inducer of antimicrobial peptide gene expression. J Immunol. 2004;173(5):2909–12. 10.4049/jimmunol.173.5.2909.
21. Xia X, Xu F, Dai D, Xiong A, Sun R, Ling Y, et al. VDR is a potential prognostic biomarker and positively correlated with immune infiltration: A comprehensive pan-cancer analysis with experimental verification. Biosci Rep. 2024;44(5):BSR20231845. 10.1042/BSR20231845.
22. Awasthi D, Sarode A. Neutrophils at the crossroads: Unraveling the multifaceted role in the tumor microenvironment. Int J Mol Sci. 2024;25(5):2929. 10.3390/ijms25052929.
23. Lee H, Kim TS, Gu JY, Yu MR, Lee SE, Kim ES, Kim HK. Value of circulating neutrophil elastase for detecting recurrence of differentiated thyroid cancer. Endocr Connect. 2023;12(12):e230400. 10.1530/EC-23-0400.
24. Lu W, Xie B, Tan G, Dai W, Ren J, Pervaz S, et al. Elafin is related to immune infiltration and could predict the poor prognosis in ovarian cancer. Front Endocrinol (Lausanne). 2023;14:1088944. 10.3389/fendo.2023.1088944.
25. Caruso JA, Akli S, Pageon L, Hunt KK, Keyomarsi K. The serine protease inhibitor elafin maintains normal growth control by opposing the mitogenic effects of neutrophil elastase. Oncogene. 2015;34(27):3556–67. 10.1038/onc.2014.284.

Figures

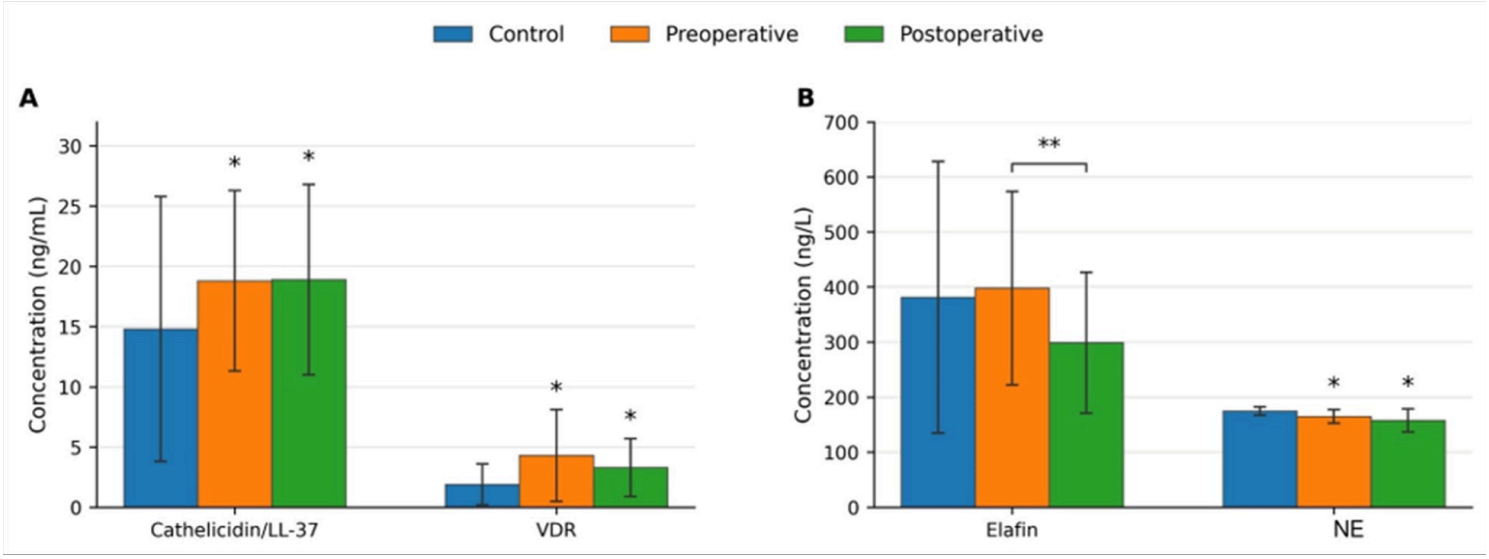

Figure 1

Serum biomarker levels in healthy controls and patients with thyroid cancer before and after surgery. (A) Serum cathelicidin/LL-37 and VDR levels (B) elafin and NE levels. Data are presented as mean ± standard deviation (SD). Preoperative and postoperative measurements were obtained from the same patients. *p<0.05 compared with the healthy control group; **p<0.05 compared with the preoperative measurement.