Periodontal inflammation and the role of C-reactive protein

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Periodontitis is a chronic and infectious inflammatory disease that leads to the destruction of the supporting structures of the teeth and includes local inflammation (1-6). Periodontal disease can induce a systemic inflammatory response associated with increased C-reactive protein (CRP) levels (7-12). Periodontitis is a multifactorial disease that occurs in bacteria, and genetic and environmental factors influence it. Proinflammatory cytokines are involved in the host immune response to periodontal pathogens through association with the inflammation phenomenon (13-20). Increased CRP levels are associated with various diseases such as cardiovascular diseases, periodontal diseases, spine and other inflammatory diseases and can be an effective biomarker for predicting future risks of periodontal diseases (21-45).

Even in healthy subjects, higher levels of serum CRP are associated with a greater risk of atherosclerosis and cardiovascular complications. CRP is one of the nonspecific mediators produced in various inflammatory situations. Its concentration increases rapidly following inflammation (1-3). It is calculated that about 10% of the adult population and about 30% of people over 50 suffer from severe

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periodontitis (1, 4, 6). As CRP is considered a major biomarker of systemic inflammation, its positive association with periodontal disease has been explored by several epidemiological, clinical and microbiological analyses (9, 10, 46, 47).

Sargolzai et al. (48) conducted a case-control study to investigate the relationship between the acute-phase reaction molecule and periodontal status, showing higher plasma concentration of CRP in the periodontal status compared with periodontally healthy subjects (control group) ($p = 0.008$). As the infective nature of periodontal diseases can affect the amount of plasma CRP, the severity of periodontitis has been positively associated with levels of CRP ≥ 0.3 mg/dL (48).

Similarly, Jayaprakash et al. (15) compared three groups (individuals with periodontitis, gingivitis and healthy group). They proved that the periodontitis group was associated with a higher mean CRP level (2.49±0.47 ng/mL) than the other 2 groups (1.40±0.32 ng/mL and 0.56±0.20 ng/mL, respectively). In addition, an interestingly significant discrepancy in CRP was observed between the gingivitis subjects and the healthy group (15).

A recent review (49) reported that chronic and aggressive periodontitis diagnoses were consistently associated with higher levels of CRP and high-sensitivity-CRP ($p<0.001$). Patients with aggressive periodontitis exhibited an average of more than 50% higher levels of CRP ($p=0.0039$) than patients with chronic periodontitis. Intensive non-intensive non-surgical periodontal treatment induced an immediate increase of high-sensitivity-CRP followed by a progressive decrease, whilst non-intensive non-surgical periodontal treatment consistently decreased high-sensitivity-CRP after treatment up to 180 days ($p<0.001$). Therefore, continuous observation with daily clinical practice by physicians and surgeons, continuous scientific research, and further discoveries can improve the long-term outcome of patients with periodontitis and other similar diseases and give them the correct clinical value for the CRP marker (50-77). Rahmati et al. (78) linked periodontal disease to systemic inflammation by showing a positive correlation between levels of CRP and immunoglobulin G of *Porphyromonas gingivalis* (*P. gingivalis*), a major bacterium colonized in the subgingival environment (79, 80).

Furthermore, limited reports suggested that control of local periodontal infection was associated with a decrease in levels of serum inflammatory markers (78). Noack et al. (18) found out that the extent of increase in CRP levels in periodontitis patients depends on the severity of the disease. They conducted a study on 174 subjects, reporting statistically significant increases in CRP levels in subjects with periodontal disease when compared to healthy controls (18). Rapone et al. (81) demonstrated significant reductions in CRP in patients who received non-surgical periodontal treatment compared with control group individuals (81). These findings provide robust evidence that periodontitis is associated with systemic inflammation as measured by serum CRP levels.

The extent of increase in CRP levels in periodontitis patients depends on the severity of the disease after adjusting for age, smoking, body mass index, triglycerides and cholesterol (18, 82-132). Investigations emphasized the role of moderate elevated CRP plasma levels as a risk factor for cardiovascular disease. Therefore, the positive correlation between CRP and periodontal disease might be a possible underlying pathway in the association between periodontal disease and the observed higher risk for cardiovascular disease in these patients. However, further studies are needed to confirm this correct association.

REFERENCES

1. Yazdi FK, Karimi N, Rasouli M, Roozbeh J. Effect of nonsurgical periodontal treatment on C-reactive protein levels in maintenance hemodialysis patients. Ren Fail. 2013;35(5):711-7. doi: 10.3109/0886022X.2013.777890. Epub 2013 Mar 28. PMID: 23534529.
2. Di Venere D, Nardi GM., Lacarbonara V, et al. Early mandibular canine-lateral incisor transposition: Case Report. Oral Implantology 2017; 10:181-189.
3. Grassi FR, Rapone B, Scarano Catanzaro F, Corsalini M, Kalemaj Z. Effectiveness of computer-assisted anesthetic delivery system (STA™) in dental implant surgery: a prospective study. Oral Implantology 2017; 10:381-389.
4. Di Venere D, Pettini F, Nardi GM, et al. Correlation

between parodontal indexes and orthodontic retainers: prospective study in a group of 16 patients. Oral Implantology 2017; 10:78-86.
5. Corsalini M, Di Venere D, Carossa M, et al. Comparative clinical study between zirconium-ceramic and metal-ceramic fixed rehabilitations. Oral Implantology 2018; 11:150–160.
6. Grassi FR, Grassi R, Rapone B, Gianfranco A, Balena A, Kalemaj Z. Dimensional changes of buccal bone plate in immediate implants inserted through open flap, open flap and bone grafting, and flapless technique. A CBCT randomized controlled clinical trial. Clin Oral Implants Res. 2019; 30:1155-1164.
7. Corsalini M, Di Venere D, Sportelli P, et al. Evaluation of prosthetic quality and masticatory efficiency in patients with total removable prosthesis: study of 12 cases. Oral Implantology 2018; 11:230–240.
8. Lorusso F, Noumbissi S, Inchingolo F, Rapone B, Khater AGA, Scarano A. Scientific Trends in Clinical Research on Zirconia Dental Implants: A Bibliometric Review. Materials 2020, 13:5534.
9. Rapone B, Converti I, Santacroce L, Cesarano F, Vecchiet F, Cacchio L, Scacco S, Grassi R, Grassi FR, Gnoni A, Nardi GM. Impact of Periodontal Inflammation on Nutrition and Inflammation Markers in Hemodialysis Patients. Antibiotics (Basel). 2019 Nov 1;8(4):209. doi: 10.3390/antibiotics8040209. PMID: 31683838; PMCID: PMC6963174.
10. Inchingolo F, Santacroce L, Ballini A, et al. Oral Cancer: A Historical Review. Int J Environ Res Public Health. 2020; 17(9):3168.
11. Corsalini M, Di Venere D, Rapone B, Stefanachi G, Laforgia A, Pettini F. Evidence of signs and symptoms of Craniomandibular Disorders in Fibromyalgia patients. The Open Dent Journal 2017; 11(1):91–98.
12. Inchingolo AD, Inchingolo AM, Bordea IR, et al. SARS-CoV-2 Disease Adjuvant Therapies and Supplements Breakthrough for the Infection Prevention. Microorganisms. 202; 9 (3):525.
13. AhmadReza Ebadian; Mehrdad Radvar; HamidReza Arab; Jalil TavakkolAfshari; Naser Sargolzaei; Salman Gharegozloo; Azam Brook; Mojhgan Shirkhani. "Analysis of Proinflammatory Cytokines Gene Polymorphisms in Generalized Aggressive Periodontitis (GAgP)". Journal of Mashhad Dental School, 33, 3, 2009, 231-240. doi: 10.22038/jmds.2009.1269
14. Kanaparthy A, Kanaparthy R, Niranjan N. Evaluation of serum C-reactive protein levels in subjects with aggressive and chronic periodontitis and comparison with healthy controls. Dent Res J (Isfahan). 2012 May;9(3):261-5. PMID: 23087729; PMCID: PMC3469890.
15. Jayaprakash D, Aghanashini S, Vijayendra RR, Chatterjee A, Rosh RM, Bharwani A. Effect of periodontal therapy on C-reactive protein levels in gingival crevicular fluid of patients with gingivitis and chronic periodontitis: A clinical and biochemical study. J Indian Soc Periodontol. 2014 Jul;18(4):456-60. doi: 10.4103/0972-124X.138688. PMID: 25210259; PMCID: PMC4158586.
16. Cozzolino M, Mangano M, Stucchi A, Ciceri P, Conte F, Galassi A. Cardiovascular disease in dialysis patients. Nephrol Dial Transplant. 2018 Oct 1;33(suppl_3):iii28-iii34. doi: 10.1093/ndt/gfy174. PMID: 30281132; PMCID: PMC6168816.
17. Kunitoshi Iseki, Masahiko Tozawa, Shinichiro Yoshi, Koshiro Fukiyama, Serum C-reactive protein (CRP) and risk of death in chronic dialysis patients, Nephrology Dialysis Transplantation, Volume 14, Issue 8, August 1999, Pages 1956–1960,
18. Noack B, Genco RJ, Trevisan M, Grossi S, Zambon JJ, De Nardin E. Periodontal infections contribute to elevated systemic C-reactive protein level. J Periodontol. 2001 Sep;72(9):1221-7. doi: 10.1902/jop.2000.72.9.1221. PMID: 11577954.
19. Rapone B, Ferrara E, Corsalini M, Converti I, Grassi FR, Santacroce L, Topi S, Gnoni A, Scacco S, Scarano A, Delvecchio M. The Effect of Gaseous Ozone Therapy in Conjunction with Periodontal Treatment on Glycated Hemoglobin Level in Subjects with Type 2 Diabetes Mellitus: An Unmasked Randomized Controlled Trial. Int. J. Environ. Res. Public Health 2020, 17(15), 54675.
20. Quaglia E, Moscufo L, Corsalini M, Coscia D, Sportelli P, Cantatore F, De Rinaldis C, Rapone B, Carossa M, Carossa S. Polyamide vs silk sutures in the healing of postextraction sockets: a split mouth study. Oral Implantology 2018 April-June; 11(2): 115-120. doi: 10.11138/orl/2018.11.2.115
21. Rapone B, Ferrara E, Santacroce L, Topi S, Gnoni A, Dipalma G, Mancini A, Di Domenico M, Tartaglia

GM, Scarano A, Inchingolo F. The Gaseous Ozone Therapy as a Promising Antiseptic Adjuvant of Periodontal Treatment: A Randomized Controlled Clinical Trial. International Journal of Environmental Research and Public Health 2022; 19(2):985.

22. Rapone B, Ferrara E, Santacroce L, et al. Periodontal Microbiological Status Influences the Occurrence of Cyclosporine-A and Tacrolimus- Induced Gingival Overgrowth. Antibiotics 2019; 8:124.
23. Montemurro N, Santoro G, Marani W, Petrella G. Posttraumatic synchronous double acute epidural hematomas: Two craniotomies, single skin incision. Surg Neurol Int. 2020; 11:435.
24. Rapone B, Ferrara E, Montemurro N, et al. Oral Microbiome and Preterm Birth: Correlation or Coincidence? A Narrative Review. Open Access Maced. J. Med. Sci. 2020; 8:123–132.
25. Rapone B, Ferrara E, Corsalini M, Qorri E, Converti I, Lorusso F, Delvecchio M, Gnoni A, Scacco S, Scarano A. Inflammatory Status and Glycemic Control Level of Patients with Type 2 Diabetes and Periodontitis: A Randomized Clinical Trial. Int J Environ Res Public Health 2021 Mar 15;18(6):3018.
26. Ballini A, Cantore S, Scacco S, et al. A comparative study on different stemness gene expression between dental pulp stem cells vs. dental bud stem cells. Eur Rev Med Pharmacol Sci. 2019; 23 (4):1626-1633.
27. Fanelli GN, Grassini D, Ortenzi V, et al. Decipher the Glioblastoma Microenvironment: The First Milestone for New Groundbreaking Therapeutic Strategies. Genes (Basel). 2021; 12 (3):445.
28. Montemurro N, Perrini P, Marani W, Chaurasia B, Corsalini M, Scarano A, Rapone B. Multiple Brain Abscesses of Odontogenic Origin. May Oral Microbiota Affect Their Development? A Review of the Current Literature. Applied Sciences. 2021; 11 (8):3316.
29. Bellocchio L, Bordea IR, Ballini A, et al. Environmental Issues and Neurological Manifestations Associated with COVID-19 Pandemic: New Aspects of the Disease? Int J Environ Res Public Health. 2020; 17 (21):8049.
30. Montemurro N, Fanelli GN, Scatena C, et al. Surgical outcome and molecular pattern characterization of recurrent glioblastoma multiforme: A single-center retrospective series. Clin Neurol Neurosurg. 2021; 207:106735.
31. Perrini P, Montemurro N. Congenital absence of a cervical spine pedicle. Neurol India. 2016; 64 (1):189-190.
32. Schroeder GD, Canseco JA, Patel PD, et al. Establishing the Injury Severity of Subaxial Cervical Spine Trauma: Validating the Hierarchical Nature of the AO Spine Subaxial Cervical Spine Injury Classification System. Spine (Phila Pa 1976). 2021; 46 (10):649-657.
33. Montemurro N, Perrini P, Rapone B. Clinical Risk and Overall Survival in Patients with Diabetes Mellitus, Hyperglycemia and Glioblastoma Multiforme. A Review of the Current Literature. Int J Environ Res Public Health. 2020; 17(22):8501.
34. Pasqualetti F, Montemurro N, Desideri I, et al. Impact of recurrence pattern in patients undergoing a second surgery for recurrent glioblastoma. Acta Neurol Belg. 2021; Aug 16.
35. Kalemaj Z, Scarano A, Valbonetti L, Rapone B, Grassi FR. Bone response to four dental implants with different surface topography: a histologic and histometric study in minipigs. Int J Periodontics Restorative Dent. 2016; 36(5):745-54.
36. Montemurro N, Perrini P. Will COVID-19 change neurosurgical clinical practice? Br J Neurosurg. 2020; 1:1-2.
37. Montemurro N. Intracranial hemorrhage and COVID-19, but please do not forget “old diseases” and elective surgery. Brain Behav Immun. 2021; 92:207-208.
38. Perrini P, Gambacciani C, Martini C, Montemurro N, Lepori P. Anterior cervical corpectomy for cervical spondylotic myelopathy: Reconstruction with expandable cylindrical cage versus iliac crest autograft. A retrospective study. Clin Neurol Neurosurg. 2015; 139:258-263.
39. Ahsan K, Khan SI, Zaman N, Ahmed N, Montemurro N, Chaurasia B. Fusion versus nonfusion treatment for recurrent lumbar disc herniation. J Craniovertebr Junction Spine. 2021; 12 (1):44-53.
40. Ahsan MK, Hossain MR, Khan MSI, et al. Lumbar revision microdiscectomy in patients with recurrent lumbar disc herniation: A single-center prospective series. Surg Neurol Int. 2020; 11:404.
41. Perrini P, Montemurro N, Caniglia M, Lazzarotti G,

Benedetto N. Wrapping of intracranial aneurysms: Single-center series and systematic review of the literature. Br J Neurosurg. 2015; 29:785-791.

42. Canseco JA, Schroeder GD, Patel PD, et al. Regional and experiential differences in surgeon preference for the treatment of cervical facet injuries: a case study survey with the AO Spine Cervical Classification Validation Group. Eur Spine J. 2021; 30 (2):517-523.
43. Montemurro N, Anania Y, Cagnazzo F, Perrini P. Survival outcomes in patients with recurrent glioblastoma treated with Laser Interstitial Thermal Therapy (LITT): A systematic review. Clin Neurol Neurosurg. 2020; 195:105942.
44. Scarano A, Inchingolo F, Murmura G, Traini T, Piattelli A, Lorusso F. Three-Dimensional Architecture and Mechanical Properties of Bovine Bone Mixed with Autologous Platelet Liquid, Blood, or Physiological Water: An In Vitro Study. Int J Mol Sci. 2018; 19 (4):1230.
45. Gnoni A, Giudetti AM. Dietary long-chain unsaturated fatty acids acutely and differently reduce the activities of lipogenic enzymes and of citrate carrier in rat liver. J Physiol Biochem. 2016 Sep;72(3):485-94.
46. Panichi V, Rizza GM, Paoletti S, Bigazzi R, Aloisi M, Barsotti G, Rindi P, Donati G, Antonelli A, Panicucci E, Tripepi G, Tetta C, Palla R; RISCAVID Study Group. Chronic inflammation and mortality in haemodialysis: effect of different renal replacement therapies. Results from the RISCAVID study. Nephrol Dial Transplant. 2008 Jul;23(7):2337-43. doi: 10.1093/ndt/gfm951. Epub 2008 Feb 27. PMID: 18305316.
47. Rapone B., Corsalini M.,Converti I., Loverro M.T., Gnoni A., Trerotoli P., Ferrara E. Does Periodontal Inflammation Affect Type 1 Diabetes in Childhood and Adolescence? A Meta-Analysis. Front. Endocrinol. 2020, 11:278. doi: 10.3389/fendo.2020.00278.
48. Sargolzai N, Moeintaghavi A, Sanatkhani M, Arab HR, Bazyar H.008. Association of Periodontal Diseases With C Reactive Protein. Journal of Medical Sciences, 2008; 8:191-195.
49. Machado V, Botelho J, Escalda C, Hussain SB, Luthra S, Mascarenhas P, Orlandi M, Mendes JJ, D'Aiuto F. Serum C-Reactive Protein and Periodontitis: A Systematic Review and Meta-Analysis. Front Immunol. 2021 Jul 28;12:706432. doi: 10.3389/fimmu.2021.706432. PMID: 34394107; PMCID: PMC8355591.
50. Condino S, Montemurro N, Cattari N, D'Amato R, Thomale U, Ferrari V, Cutolo F. Evaluation of a Wearable AR Platform for Guiding Complex Craniotomies in Neurosurgery. Ann Biomed Eng. 2021; 49 (9):2590-2605.
51. Montemurro N, Condino S, Cattari N, D'Amato R, Ferrari V, Cutolo F. Augmented Reality-Assisted Craniotomy for Parasagittal and Convexity En Plaque Meningiomas and Custom-Made Cranio-Plasty: A Preliminary Laboratory Report. Int J Environ Res Public Health. 2021; 18 (19):9955.
52. Cantore S, Ballini A, De Vito D, et al. Characterization of human apical papilla-derived stem cells. J Biol Regul Homeost Agents. 2017; 31 (4):901-910.
53. Lizana J, Montemurro N, Aliaga N, Marani W, Tanikawa R. From textbook to patient: a practical guide to train the end-to-side microvascular anastomosis. Br J Neurosurg. 2021; 7:1-5.
54. Rapone B, Nardi GM, Di Venere D, Pettini F, Grassi FR, Corsalini M. Oral hygiene in patients with oral cancer undergoing chemotherapy and/or radiotherapy after prosthesis rehabilitation: protocol proposal. Oral Implantology 2016; 9 (01 suppl): 90-97.
55. Inchingolo F, Ballini A, Cagiano R, et al. Immediately loaded dental implants bioactivated with platelet-rich plasma (PRP) placed in maxillary and mandibular region. Clin Ter. 2015; 166 (3):e146-52.
56. Inchingolo F, Tatullo M, Abenavoli FM, et al. Severe anisocoria after oral surgery under general anesthesia. Int J Med Sci. 2010; 7 (5):314-8.
57. Inchingolo F, Tatullo M, Pacifici A, et al. Use of dermal-fat grafts in the post-oncological reconstructive surgery of atrophies in the zygomatic region: clinical evaluations in the patients undergone to previous radiation therapy. Head Face Med. 2012; 8:33.
58. Inchingolo F, Tatullo M, Abenavoli FM, et al. Surgical treatment of depressed scar: a simple technique. Int J Med Sci. 2011;8(5):377-9.
59. Lizana J, Reinoso CMD, Aliaga N, Marani W, Montemurro N. Bilateral central retinal artery

occlusion: An exceptional complication after frontal parasagittal meningioma resection. Surg Neurol Int. 2021; 12:397.
60. Montemurro N, Scerrati A, Ricciardi L, Trevisi G. The Exoscope in Neurosurgery: An Overview of the Current Literature of Intraoperative Use in Brain and Spine Surgery. J Clin Med. 2021; 11 (1):223.
61. Marani W, Mannará F, Noda K, et al. Management of an Uncommon Complication: Anterior Choroidal Artery Occlusion by Posterior Clinoid Process Detected Through Intraoperative Monitoring After Clipping of Paraclinoid Aneurysm: 2-Dimensional Operative Video. Oper Neurosurg (Hagerstown). 2021; 21 (2):E124-E125.
62. Montemurro N, Herbet G, Duffau H. Right Cortical and Axonal Structures Eliciting Ocular Deviation During Electrical Stimulation Mapping in Awake Patients. Brain Topogr. 2016; 29 (4):561-571.
63. Borsani E, Bonazza V, Buffoli B, et al. Beneficial Effects of Concentrated Growth Factors and Resveratrol on Human Osteoblasts In Vitro Treated with Bisphosphonates. Biomed Res Int. 2018; 2018:4597321.
64. Montemurro N. Glioblastoma Multiforme and Genetic Mutations: The Issue Is Not Over Yet. An Overview of the Current Literature. J Neurol Surg A Cent Eur Neurosurg. 2020; 81 (1):64-70.
65. Di Venere D, Corsalini M, Nardi GM, Laforgia A, Grassi FR, Rapone B, Pettini F. Obstructive site localization in patients with Obstructive Sleep Apnea Syndrome: a comparison between otolaryngologic data and cephalometric values. Oral Implantology 2017; 10:295–310.
66. Murrone D, Romanelli B, Montemurro N, Chirchiglia D, Ierardi A. Falcine meningioma in Von Hippel-Lindau disease: An unusual association. Surg Neurol Int. 2018; 9:37.
67. Montemurro N, Perrini P, Mangini V, Galli M, Papini A. The Y-shaped trabecular bone structure in the odontoid process of the axis: a CT scan study in 54 healthy subjects and biomechanical considerations. J Neurosurg Spine. 2019; 1:1-8.
68. Benet A, Montemurro N, Lawton MT. Management of a Ruptured Posterior Inferior Cerebellar Artery (PICA) Aneurysm With PICA-PICA In Situ Bypass and Trapping: 3-Dimensional Operative Video. Oper Neurosurg (Hagerstown). 2017; 13 (3):400.
69. Owen CM, Montemurro N, Lawton MT. Blister Aneurysms of the Internal Carotid Artery: Microsurgical Results and Management Strategy. Neurosurgery. 2017; 80 (2):235-247.
70. Montemurro N, Perrini P, Blanco MO, Vannozzi R. Second surgery for recurrent glioblastoma: A concise overview of the current literature. Clin Neurol Neurosurg. 2016; 142:60-64.
71. Owen CM, Montemurro N, Lawton MT. Microsurgical Management of Residual and Recurrent Aneurysms After Coiling and Clipping: An Experience With 97 Patients. Neurosurgery. 2015; Suppl 1:92-102.
72. Perrini P, Montemurro N, Iannelli A. The contribution of Carlo Giacomini (1840-1898): the limbus Giacomini and beyond. Neurosurgery. 2013; 72 (3):475-481.
73. Montemurro N, Benet A, Lawton MT. Julius Caesar's Epilepsy: Was It Caused by A Brain Arteriovenous Malformation? World Neurosurg. 2015; 84 (6):1985-1987.
74. Montemurro N, Perrini P, Vannozzi R. Epidural spinal cord compression in Langerhans cell histiocytosis: a case report. Br J Neurosurg. 2013; 27 (6):838-839.
75. Canseco JA, Schroeder GD, Paziuk TM, et al. The Subaxial Cervical AO Spine Injury Score. Global Spine J. 2020; 11:2192568220974339.
76. Benedetto N, Gambacciani C, Montemurro N, Morganti R, Perrini P. Surgical management of acute subdural haematomas in elderly: report of a single center experience. Br J Neurosurg. 2017; 31 (2):244-248.
77. Montemurro N, Benet A, Lawton MT. Clipping of Ruptured Residual Anterior Communicating Artery Aneurysm After Endovascular Coiling: 3-Dimensional Operative Video. Oper Neurosurg (Hagerstown). 2016; 12 (1):93-94.
78. Rahmati MA, Craig RG, Homel P, Kaysen GA, Levin NW. Serum markers of periodontal disease status and inflammation in hemodialysis patients. Am J Kidney Dis. 2002; 40 (5):983-9.
79. Cekici A, Kantarci A, Hasturk H, Van Dyke TE. Inflammatory and immune pathways in the pathogenesis of periodontal disease. Periodontol 2000. 2014 Feb;64(1):57-80. doi: 10.1111/prd.12002.

PMID: 24320956; PMCID: PMC4500791.

80. Charitos IA, Ballini A, Bottalico L, Cantore S, Passarelli PC, Inchingolo F, D'Addona A, Santacroce L. Special features of SARS-CoV-2 in daily practice. World J Clin Cases. 2020; 8 (18):3920-3933.
81. Rapone B, Ferrara E, Santacroce L, Topi S, Converti I, Gnoni A, Scarano A, Scacco S. Gingival Crevicular Blood as a Potential Screening Tool: A Cross Sectional Comparative Study. Int J Environ Res Public Health. 2020 Oct 9;17(20):7356. doi: 10.3390/ijerph17207356. PMID: 33050132; PMCID: PMC7601154.
82. Scarano, A.; Inchingolo, F.; Rapone, B.; Festa, F.; Tari, S.R.; Lorusso, F. Protective Face Masks: Effect on the Oxygenation and Heart Rate Status of Oral Surgeons during Surgery. Int. J. Environ. Res. Public Health 2021, 18, 2363.
83. Inchingolo F, Martelli FS, Gargiulo Isacco C, et al. Chronic Periodontitis and Immunity, Towards the Implementation of a Personalized Medicine: A Translational Research on Gene Single Nucleotide Polymorphisms (SNPs) Linked to Chronic Oral Dysbiosis in 96 Caucasian Patients. Biomedicines. 2020; 8(5):115.
84. Rapone B., Palmisano C., Ferrara E., Di Venere D., Albanese G., Corsalini M. The Accuracy of Three Intraoral Scanners in the Oral Environment with and without Saliva: A Comparative Study. *Appl. Sci.* 2020, *10*(21), 7762.
85. Santacroce L, Inchingolo F, Topi S, Del Prete R, Di Cosola M, Charitos IA, Montagnani M. Potential beneficial role of probiotics on the outcome of COVID-19 patients: An evolving perspective. Diabetes Metab Syndr. 2021; 15 (1):295-301.
86. Ballini A, Cantore S, Scacco S, et al. A comparative study on different stemness gene expression between dental pulp stem cells vs. dental bud stem cells. Eur Rev Med Pharmacol Sci. 2019; 23 (4):1626-1633.
87. Cantore S, Ballini A, De Vito D, et al. Characterization of human apical papilla-derived
88. Inchingolo F, Tatullo M, Abenavoli FM, Marrelli M, Inchingolo AD, Inchingolo AM, Dipalma G. Comparison between traditional surgery, CO2 and Nd:Yag laser treatment for generalized gingival hyperplasia in Sturge-Weber syndrome: a retrospective study. J Investig Clin Dent. 2010; 1 (2):85-89.
89. Dang QT, Huynh TD, Inchingolo F, Dipalma G, Inchingolo AD, et al. Human Chondrocytes from Human Adipose Tissue-Derived Mesenchymal Stem Cells Seeded on a Dermal-Derived Collagen Matrix Sheet: Our Preliminary Results for a Ready to Go Biotechnological Cartilage Graft in Clinical Practice. Stem Cells Int. 2021; 2021:6664697.
90. Ballini A, Cantore S, Signorini L, Saini R, Scacco S, Gnoni A, Inchingolo AD, et al. Efficacy of Sea Salt-Based Mouthwash and Xylitol in Improving Oral Hygiene among Adolescent Population: A Pilot Study. Int J Environ Res Public Health. 2020; 18 (1):44.
91. Adina S, Dipalma G, Bordea IR, Lucaciu O, Feurdean C, Inchingolo AD, et al. Orthopedic joint stability influences growth and maxillary development: clinical aspects. J Biol Regul Homeost Agents. 2020; 34 (3):747-756.
92. Pham VH, Gargiulo Isacco C, Nguyen KCD, et al. Rapid and sensitive diagnostic procedure for multiple detection of pandemic Coronaviridae family members SARS-CoV-2, SARS-CoV, MERS-CoV and HCoV: a translational research and cooperation between the Phan Chau Trinh University in Vietnam and University of Bari "Aldo Moro" in Italy. Eur Rev Med Pharmacol Sci. 2020; 24 (12):7173-7191.
93. Bordea IR, Xhajanka E, Candrea S, Bran S, Onişor F, Inchingolo AD, et al. Coronavirus (SARS-CoV-2) Pandemic: Future Challenges for Dental Practitioners. Microorganisms. 2020; 8 (11):1704.
94. Farronato, M.; Farronato, D.; Inchingolo, F.; Grassi, L.; Lanteri, V.; Maspero, C. Evaluation of Dental Surface after De-Bonding Orthodontic Bracket Bonded with a Novel Fluorescent Composite: In Vitro Comparative Study. Appl. Sci. 2021, 11, 6354, doi:10.3390/app11146354.
95. Cardarelli, F.; Patano, A.; Montenegro, V.; Malcangi, G.; Coloccia, G.; Inchingolo, A.D.; Marinelli, G.; Laudadio, C.; Dipalma, G.; Di Venere, D.; Inchingolo, F. Elastodontic therapy un nuovo approccio alla terapia ortodontica funzionale. Il Dentista Moderno 2021, 48-63
96. Inchingolo, F.; Tatullo, M.; Marrelli, M.; Inchingolo, A.M.; Tarullo, A.; Inchingolo, A.D.; Dipalma, G.; Brunetti, S.P.; Tarullo, A.; Cagiano, R. Combined

Occlusal and Pharmacological Therapy in the Treatment of Temporo-Mandibular Disorders. Eur. Rev. Med. Pharmacol. Sci. 2011, 15, 1296–1300.

97. Topi S, Santacroce L, Bottalico L, Ballini A, Inchingolo AD, Dipalma G, Charitos IA, Inchingolo F. Gastric Cancer in History: A Perspective Interdisciplinary Study. Cancers (Basel). 2020 Jan 22;12(2):264. doi: 10.3390/cancers12020264.
98. Boccellino M, Di Stasio D, Dipalma G, Cantore S, Ambrosio P, Coppola M, Quagliuolo L, Scarano A, Malcangi G, Borsani E, Rinaldi B, Nuzzolese M, Xhajanka E, Ballini A, Inchingolo F, Di Domenico M. Steroids and growth factors in oral squamous cell carcinoma: useful source of dental-derived stem cells to develop a steroidogenic model in new clinical strategies. Eur Rev Med Pharmacol Sci. 2019 Oct;23(20):8730-8740. doi: 10.26355/eurrev_201910_19267.
99. Vermesan D, Inchingolo F, Patrascu JM, Trocan I, Prejbeanu R, Florescu S, Damian G, Benagiano V, Abbinante A, Caprio M, Cagiano R, Haragus H. Anterior cruciate ligament reconstruction and determination of tunnel size and graft obliquity. Eur Rev Med Pharmacol Sci. 2015;19(3):357-64.
100. Inchingolo F, Tatullo M, Abenavoli FM, Marrelli M, Inchingolo AD, Corelli R, Inchingolo AM, Dipalma G. Upper eyelid reconstruction: a short report of an eyelid defect following a thermal burn. Head Face Med. 2009 Nov 25;5:26. doi: 10.1186/1746-160X-5-26.
101. Inchingolo F, Pacifici A, Gargari M, Acitores Garcia JI, Amantea M, Marrelli M, Dipalma G, Inchingolo AM, Rinaldi R, Inchingolo AD, Pacifici L, Tatullo M. CHARGE syndrome: an overview on dental and maxillofacial features. Eur Rev Med Pharmacol Sci. 2014;18(15):2089-93.
102. Inchingolo F, Tatullo M, Abenavoli FM, Inchingolo AD, Inchingolo AM, Dipalma G. Fish-hook injuries: a risk for fishermen. Head Face Med. 2010 Dec 14;6:28. doi: 10.1186/1746-160X-6-28.
103. Borsani E, Bonazza V, Buffoli B, Nocini PF, Albanese M, Zotti F, Inchingolo F, Rezzani R, Rodella LF. Beneficial Effects of Concentrated Growth Factors and Resveratrol on Human Osteoblasts *In Vitro* Treated with Bisphosphonates. Biomed Res Int. 2018 May 16;2018:4597321. doi: 10.1155/2018/4597321.
104. Fanali S, Tumedei M, Pignatelli P, Inchingolo F, Pennacchietti P, Pace G, Piattelli A. Implant primary stability with an osteocondensation drilling protocol in different density polyurethane blocks. Comput Methods Biomech Biomed Engin. 2021 Jan;24(1):14-20. doi: 10.1080/10255842.2020.1806251.
105. Dohan Ehrenfest, D.M., Del Corso, M., Inchingolo, F., Charrier, J.-B. Selecting a relevant in vitro cell model for testing and comparing the effects of a Choukroun's platelet-rich fibrin (PRF) membrane and a platelet-rich plasma (PRP) gel: Tricks and traps. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology, 2010, 110(4), pp. 409–411.
106. Inchingolo F, Tatullo M, Marrelli M, Inchingolo AD, Corelli R, Inchingolo AM, Dipalma G, Abenavoli FM. Clinical case-study describing the use of skin-perichondrium-cartilage graft from the auricular concha to cover large defects of the nose. Head Face Med. 2012 Mar 19;8:10. doi: 10.1186/1746-160X-8-10.
107. Inchingolo F, Tatullo M, Abenavoli FM, Marrelli M, Inchingolo AD, Servili A, Inchingolo AM, Dipalma G. A hypothetical correlation between hyaluronic acid gel and development of cutaneous metaplastic synovial cyst. Head Face Med. 2010 Jul 15;6:13. doi: 10.1186/1746-160X-6-13.
108. Goldoni R, Dolci C, Boccalari E, Inchingolo F, Paghi A, Strambini L, Galimberti D, Tartaglia GM. Salivary biomarkers of neurodegenerative and demyelinating diseases and biosensors for their detection. Ageing Res Rev. 2022 Apr;76:101587. doi: 10.1016/j.arr.2022.101587.
109. Ceratti C, Maspero C, Consonni D, Caprioglio A, Connelly ST, Inchingolo F, Tartaglia GM. Cone-Beam Computed Tomographic Assessment of the Mandibular Condylar Volume in Different Skeletal Patterns: A Retrospective Study in Adult Patients. Bioengineering (Basel). 2022 Mar 2;9(3):102.
110. Maspero C, Cappella A, Dolci C, Cagetti MG, Inchingolo F, Sforza C. Is Orthodontic Treatment with Microperforations Worth It? A Scoping Review. Children (Basel). 2022 Feb 6;9(2):208.
111. Cantore, S., Ballini, A., De Vito, D., et al. Clinical results of improvement in periodontal condition by administration of oral Probiotics. Journal of

Biological Regulators and Homeostatic Agents, 2018, 32(5), pp. 1329–1334.

112. Lorusso F, Postiglione F, Delvecchio M, Rapone B., Scarano A. The impact of diabetes on implant oral rehabilitations: a bibliometric study and literature review. Acta Medica Mediterranea 2020; 36: 3333.
113. Di Comite M, Crincoli V, Fatone L, Ballini A, et al. Quantitative analysis of defects at the dentin-post space in endodontically treated teeth. Materials 2015; 8,3268-3283.
114. Scarola R, Montemurro N, Ferrara E, Corsalini M, Converti I, Rapone B. Temporomandibular Disorders and Fibromyalgia: A Narrative Review. Open Access Maced J Med Sci [Internet]. 2021; 9 (F):106-12.
115. Rapone B, Pedone S, Carnevale A, Plantamura P, Scarano A, Demelio A, Demelio GP, Corsalini M. Profilometer Comparison of the Surface Roughness of Four Denture Base Resins: An In Vitro Study. Applied Sciences. 2022; 12(4):1837. https://doi.org/10.3390/app12041837.
116. Malcangi G, Inchingolo AD, Inchingolo AM, Piras F, Settanni V, Garofoli G, Palmieri G, Ceci S, Patano A, Mancini A, Vimercati L, Nemore D, Scardapane A, Rapone B, Semjonova A, D'Oria MT, Macchia L, Bordea IR, Migliore G, Scarano A, Lorusso F, Tartaglia GM, Giovanniello D, Nucci L, Maggialetti N, Parisi A, Domenico MD, Brienza N, Tafuri S, Stefanizzi P, Curatoli L, Corriero A, Contaldo M, Inchingolo F, Dipalma G. COVID-19 Infection in Children and Infants: Current Status on Therapies and Vaccines. Children. 2022; 9(2):249. https://doi.org/10.3390/children9020249.
117. Malcangi G, Inchingolo AD, Patano A, Coloccia G, Ceci S, Garibaldi M, Inchingolo AM, Piras F, Cardarelli F, Settanni V, Rapone B, Corriero A, Mancini A, Corsalini M, Nucci L, Bordea IR, Lorusso F, Scarano A, Giovanniello D, Dipalma G, Posa VM, Di Venere D, Inchingolo F. Impacted Central Incisors in the Upper Jaw in an Adolescent Patient: Orthodontic-Surgical Treatment-A Case Report. Applied Sciences. 2022; 12(5):2657. https://doi.org/10.3390/app12052657.
118. Di Venere D, Rapone B, Corsalini M. Dental trauma in the anterior sector: an analysis of the predisposing factors in a group of orthodontic patients. Clinica Terapeutica 2020, 171 (6):e481-485. doi: 10.7417/CT.2020.2261.
119. Nardi G.M., Ferrara E., Converti I., Cesarano F., Scacco S., Grassi R., Gnoni A., Grassi F.R., Rapone B. Does Diabetes Induce the Vascular Endothelial Growth Factor (VEGF) Expression in Periodontal Tissues? A Systematic Review. Int. J. Environ. Res. Public Health 2020, 17(8), 2765. doi: 10.3390/ijerph17082765.
120. Inchingolo, A.D.; Ceci, S.; Patano, A.; Inchingolo, A.M.; Montenegro, V.; Di Pede, C.; Malcangi, G.; Marinelli, G.; Coloccia, G.; Garibaldi, M.; Kruti, Z.; Palmieri, G.; De Leonardis, N.; Rapone, B.; Mancini, A.; Semjonova, A.; Nucci, L.; Bordea, I.R.; Scarano, A.; Lorusso, F.; Ferrara, E.; Farronato, M.; Tartaglia, G.M.; Di Venere, D.; Cardarelli, F.; Inchingolo, F.; Dipalma, G. Elastodontic Therapy of Hyperdivergent Class II Patients Using AMCOP® Devices: A Retrospective Study. *Appl. Sci.*2022, *12*, 3259. doi: 10.3390/app12073259
121. Di Naro E, Loverro M, Converti I, Loverro MT, Ferrara E, Rapone B. The Effect of Menopause Hypoestrogenism on Osteogenic Differentiation of Periodontal Ligament Cells (PDLC) and Stem Cells (PDLCs): A Systematic Review. Healthcare (Basel). 2021 May 12;9(5):572. doi: 10.3390/healthcare9050572.
122. Mavriqi L, Lorusso F, Conte R, Rapone B, Scarano A. Zygomatic implant penetration to the central portion of orbit: a case report. BMC Ophthalmol. 2021, 21(1):121. doi: 10.1186/s12886-021-01846-1.
123. Corsalini M, Rapone B, Cagnetta G, Carossa M, Sportelli P, De Giacomo A, Laforgia A, Di Venere D. Orofacial functions and chewing effiency in elderly patients with Parkinsons's disease rehabilitated with removable prostheses. The Open Dentistry 2020, 14:13-18. doi: 10.2174/1874210602014010013.
124. Scarano A, Rapone B, Amuso D, Inchingolo F, Lorusso F. Hyaluronic Acid Fillers Enriched with Glycine and Proline in Eyebrow Augmentation Procedure. Aesthetic Plast Surg. 2022 Feb;46(1):419-428. doi: 10.1007/s00266-021-02412-2.
125. Scarano A., Inchingolo F., Rapone B., Lucchina A.G., Qorri E., Lorusso F. Role of Autologous Platelet Gel (APG) in Bone Healing: A Rabbit Study. Appl. Sci. 2021, 11, 395. doi: 10.3390/app11010395.
126. Delvecchio M, Rapone B, Simonetti S, Fecarotta S,

De Carlo G, Favoino E, Loverro MT, Romano AMI, Taurino F, Di Naro E, Gnoni A. Dietary cholesterol supplementation and inhibitory factor 1 serum levels in two dizygotic Smith-Lemli-Opitz syndrome twins: a case report. Ital J Pediatr. 2020 Oct 28;46(1):161. doi: 10.1186/s13052-020-00924-2.

127. Corsalini M, Rapone B, Grassi FR, Di Venere D. A study on oral rehabilitation in stroke patients: analysis of a group of 33 patients. Gerodontology. 2010 Sep;27(3):178-82. doi: 10.1111/j.1741-2358.2009.00322.x.
128. Kalemaj Z, Scarano A, Valbonetti L, Rapone B, Grassi FR. Bone Response to Four Dental Implants with Different Surface Topographies: A Histologic and Histometric Study in Minipigs. Int J Periodontics Restorative Dent. 2016 Sep-Oct;36(5):745-54. doi: 10.11607/prd.2719.
129. Rapone B, Inchingolo AD, Trasarti S, Ferrara E, Qorri E, Mancini A, Montemurro N, Scarano A, Inchingolo AM, Dipalma G, Inchingolo F. Long-Term Outcomes of Implants Placed in Maxillary Sinus Floor Augmentation with Porous Fluorohydroxyapatite (Algipore® FRIOS®) in Comparison with Anorganic Bovine Bone (Bio-Oss®) and Platelet Rich Plasma (PRP): A Retrospective Study. *Journal of Clinical Medicine*. 2022; 11(9):2491.
130. Inchingolo AD, Patano A, Coloccia G, Ceci S, Inchingolo AM, Marinelli G, Malcangi G, Di Pede C, Garibaldi M, Ciocia AM, Mancini A, Palmieri G, Rapone B, Piras F, Cardarelli F, Nucci L, Bordea IR, Scarano A, Lorusso F, Giovanniello D, Costa S, Tartaglia GM, Di Venere D, Dipalma G, Inchingolo F. Treatment of Class III Malocclusion and Anterior Crossbite with Aligners: A Case Report. Medicina. 2022; 58(5):603.
131. Inchingolo AD, Malcangi G, Inchingolo AM, Piras F, Settanni V, Garofoli G, Palmieri G, Ceci S, Patano A, De Leonardis N, Di Pede C, Montenegro V, Azzollini D, Garibaldi MG, Kruti Z, Tarullo A, Coloccia G, Mancini A, Rapone B et al. Benefits and Implications of Resveratrol Supplementation on Microbiota Modulations: A Systematic Review of the Literature. International Journal of Molecular Sciences. 2022; 23(7):4027.
132. Lorusso, F.; Postiglione, F.; Delvecchio, M.; Rapone, B.; Scarano, A. The impact of diabetes in implant oral rehabilitations: A bibliometric study and literature review. Acta Med. Mediterr. 2020, 36, 3333.