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REVIEW

Medico-legal considerations in immediate loading implantology: risks, responsibilities, and best practices

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ABSTRACT

The field of immediate loading implantology has grown rapidly, offering quicker solutions for prosthetic rehabilitation. However, the complexity of this technique raises significant medico-legal concerns regarding patient safety, treatment planning, and professional liability. These issues are particularly relevant in elective procedures where failure could lead to litigation. A comprehensive review of current literature, including clinical studies, legal rulings, and malpractice claims, was conducted to assess the legal implications of immediate loading implantology. The analysis focused on professional liability, patient consent, and complications during treatment. The evidence indicates that a high standard of care, including detailed preoperative planning, risk assessment, and clear patient communication, is essential in minimizing legal risks. Malpractice claims often arise from inadequate patient information or failure to follow established protocols. Proper documentation of informed consent and adherence to evidence-based dentistry (EBD) guidelines are crucial to protect both patients and practitioners. Immediate loading implantology offers numerous benefits, but it requires meticulous planning and patient management to avoid medico-legal issues. Ensuring comprehensive patient consent and following evidence-based practices are key to reducing professional liability and improving outcomes. Further studies should explore standardized protocols for reducing complications and legal disputes in implantology.

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The issue of dental professional liability is situated within the broader context of medical professional liability, which itself is embedded in an ethical, regulatory, and economic framework that has undergone significant changes in recent years. These changes have inevitably influenced the criteria for attributing and assessing liability, particularly civil liability, within the healthcare

professions. Among the factors contributing to the revision of the aforementioned criteria, in response to the increasing prevalence of malpractice claims, is the shift (particularly in certain disciplines such as dentistry) of the focus of medical practice towards so-called 'elective' treatments, aimed at addressing the growing demand for improved quality of life.

Similarly, the use of increasingly sophisticated diagnostic and therapeutic techniques contributes to reducing errors but also introduces a dynamic aspect to the risk of malpractice, which is closely linked to scientific and technological advancements.[1]

Additionally, it is important to consider the evolution in the relationship between physician/dentist and patient over the past twenty years. The previously 'paternalistic' attitude has given way to a condition of absolute balance between the parties, with an increase in the population's awareness of their rights and knowledge about contemporary medical possibilities. This information is readily accessible through online portals and mass media, though it is often unrealistic and lacking solid scientific foundations, as seen with experimental research and techniques that are sometimes prematurely publicized.[2]

In this context, there has been an increase in cases of professional liability, particularly noticeable in the field of dentistry, where, as is well known, a contractual relationship is established between the practitioner and the patient.

This relationship (Article 1218 of the Italian Civil Code) stipulates that, in the event of a performance not being correctly executed, the debtor (the medical practitioner or dentist) is liable for damages, unless they can demonstrate that the non-fulfillment or delay is due to a cause not attributable to them. This principle also applies to advanced techniques that offer better results compared to traditional methods.

Indeed, if there is an intrinsic risk associated with such procedures, the healthcare provider assumes responsibility for that risk in addition to any potential errors.[1, 3]

If there is an intrinsic risk associated with such procedures, the healthcare provider assumes responsibility for that risk in addition to any potential errors. Therefore, it is important to differentiate between errors, complications, and unforeseeable events, which are often confused or misinterpreted by those evaluating medical practice. Medicine is a complex science and is not free from complications and unforeseen circumstances.

First, it is necessary to distinguish between "true errors," which are undeniably evident, and "apparent errors," which are deemed inappropriate and disadvantageous only *a posteriori*, but which fall within the realm of the unpredictable.[3, 4]

Complications arising from medical treatment do not necessarily constitute errors; however, to rule out this possibility, it is essential to verify in advance whether the treatment was properly planned, suitable for the specific case, and whether any pre-existing conditions were appropriately evaluated. Furthermore, any complications that arose should have been adequately diagnosed and managed.

An unforeseeable event implies the exclusion of culpability (Article 45 of the Italian Penal Code) and occurs when the event is the result of unpredictable, unavoidable, and thus imponderable circumstances (*e.g.*, an unexpected allergic reaction; accidental ingestion of a temporary element).

The evaluation of negligent responsibility as a consequence of foreseeable complications inherent to the disease or the applied therapy is more complex. In such cases, it is necessary to assess, on a case-by-case basis, whether and to what extent the physician took all necessary precautions to prevent the adverse event from occurring.

Thus, it can be asserted that errors leading to liability include: diagnostic errors, when a pathological condition has not been correctly interpreted, distinguishing the stages in which the error may occur. Specifically, the empirical stage, characterized by an imprecise or inadequate medical history, an incomplete physical examination, or incorrect or misinterpreted instrumental and laboratory tests, and the rational stage, in which the critical analysis of the available data is fragmented or erroneous, resulting in an incorrect or missed diagnosis.

Prognostic and therapeutic errors may also arise from these, with the latter including mis-

takes in the technical execution of the treatment. An error results from negligent behavior leading to an unintended event (patient harm) due to negligence, imprudence, or lack of skill – referred to as general negligence – or due to non-compliance with laws, regulations, orders, or standards (specific negligence).

Specifically, negligence is generally characterized by an omission, particularly the neglect of certain precautions that any competent professional should adopt, relative to the level of scientific advancement and technical measures available at the time the service was provided.

In this context, it is emphasized that failing to formulate an accurate diagnostic judgment due to omissions in necessary investigations or incorrect evaluation of their results is among the most common causes of professional liability disputes. Imprudence, on the other hand, involves behavior characterized by superficiality or recklessness, such as performing treatments hastily despite recognizing a lack of appropriate resources or skills for the specific case. Lack of skill manifests as a technical error due to incompetence, inadequate preparation, or insufficient ability.

However, while there is a categorical imperative for physicians regarding the requirements of "diligence" and "prudence," jurisprudence is clear that "the assessment of professional fault of the healthcare provider must be made with a broad perspective and understanding of the peculiarities of medical practice and the difficulty of specific cases." Article 2236 of the Civil Code specifies that in cases involving the resolution of technically complex problems, liability for lack of skill is only attributed in cases of "gross negligence."[5, 6]

Conversely, as previously mentioned, when a professional's liability arises from a lack of diligence or prudence, "the assessment must consider the nature of the activity performed, with the result that even slight negligence is relevant, as the diligence required is that of a careful professional who conducts their activities with meticulous attention and adequate preparation" (Criminal Court of Cassation).

These general principles provide a backdrop for discussing the more specific issue of dentist liability in implant treatment, particularly in immediate loading procedures. The replacement of missing teeth with prosthetic devices has always been a primary objective in dentistry.

In particular, regarding implantology, the idea of prosthetically replacing the root of missing teeth has been experimented with using various methods (endodontic implants, intramucosal inserts, subperiosteal implants, blades, screws, and endosseous cylinders). It achieved scientific validity only in recent times, thanks to Brånemark, who, based on the principle of osseointegration, introduced highly biocompatible materials and effective, standardized procedures into implant surgery. This established implantology as a significant option among various types of prosthetics aimed at restoring the function and aesthetics of patients with dental deficiencies.

The undeniable advantages demonstrated by implant-supported prostheses in certain conditions of edentulism have contributed to their progressive and widespread adoption. This, in turn, has led to the emergence of new cases of litigation, based on malpractice allegations from dissatisfied patients or, in some cases, motivated by the prospect of attractive compensation.

The field of implantology, due to its unique characteristics, presents a range of medico-legal considerations. These are 'elective' procedures, as previously mentioned, which are not typically characterized by urgency and usually offer the possibility of an alternative therapeutic approach, such as traditional prosthetics. Additionally, in some situations the distinction between the operator's responsibility and the unpredictability of the patient's response to the treatment can be quite blurred.

Given that these are invasive procedures that are never urgent or necessary, the primary medico-legal issue is assessing the patient's actual suitability for implant surgical treatment.[7]

In other words, the use of this type of technique cannot be justified merely by the operator's preference or the patient's persistent request. It requires a rigorous selection process to exclude the presence of general or local contraindications that could lead to treatment failure or, worse, expose the patient to the risk of severe complications.

General and absolute contraindications include severe systemic or cardiac diseases, blood dyscrasias, altered hemostasis, use of anticoagulants, and uncontrolled diabetes. Local contraindications primarily involve insufficient bone thickness in relation to anatomical structures such as the maxillary sinus, nasal cavities, and mandibular canal, unless preceded by bone grafting or tissue regeneration techniques. Other local contraindications include active periodontal diseases, neoplasms, severe smoking habits, and poor oral hygiene.

Therefore, a preliminary investigation into the patient's general health and oral cavity conditions is essential, including radiological assessments and, in borderline cases, densitometric evaluations (such as dentascan). These assessments allow for the evaluation of both the quantity and quality of the bone. It should be noted that if a failure is attributable to inadequate initial evaluation, it will be challenging for the dentist to avoid liability.

Regarding implant treatment failures, they can be simply categorized into intraoperative incidents and long-term therapeutic failures. The former, depending on the extent of the injuries, may cause temporary or permanent damage, identifiable as iatrogenic disease, typically of an inflammatory-infective nature, potentially leading to chronic conditions or anatomical-functional outcomes.

In this context, consider neurological injuries (particularly to the inferior alveolar nerve), injuries to tissues adjacent to the implant site (such as invasion of the maxillary sinus or piriform cavities), or infectious complications (such as maxillary sinusitis, ethmoiditis, oroantral communications) attributable to contamination or incorrect placement of implants.

In these situations, demonstrating professional error is not particularly challenging, especially if the adverse event results from a superficial evaluation of the patient's initial conditions or the omission of instrumental investigations that could provide useful indications to prevent the incident.

In reference to this, a 2000 ruling (No. 5945) by the court of cassation stated that medical professional liability 'exists not only in cases of gross negligence or intent by the healthcare provider, but also in instances of minor negligence when, in a routine case, the provider fails to follow the established rules acquired through extensive experimentation in medical practice, which the specialist should not be unaware of.

This statement inevitably highlights the contentious issue of whether implantology should be classified among the procedures that involve solving technically challenging problems.

In our view, given increasingly reliable operational protocols and the constant development in the field, except for rare exceptions, implant surgery cannot be considered inherently of special difficulty, where 'special difficulty' refers to solving complex cases that necessitate the use of therapeutic methods that have not been sufficiently studied or tested.

Cases of therapeutic failure, such as early or late loss of the implant, require a detailed analysis to identify possible causes and determine or exclude the responsibility of the operator.

Generally, failures are more frequently attributed to peri-implant infections, failure of osseointegration, inadequacy of endosseous implants (in terms of diameter, shape, length relative to the surgical site), or inadequate relationships between the implant and prosthesis (in terms of number, position, and/or angulation).

In all these cases, implant loss is also accompanied by alterations in the bone structure, including substance loss attributable to osteolytic phenomena, further exacerbated by the procedures for implant removal.[8]

This situation implies that, if the operator's responsibility for the adverse event is established, they could be held liable for personal injury in criminal proceedings or be required to compensate for health-related and economic damages in civil proceedings.[8]

In this regard, consider the case of implant loss following peri-implant infections. It is necessary to determine whether the failure was due to the presence of untreated infectious foci near the surgical site, which would imply negligence on the part of the professional (as it is good practice to eliminate all potential sources of bacterial contamination before the surgical procedure), or if it was caused by patient neglect, such as miss-

ing periodic check-ups or failing to correctly use the prescribed home oral hygiene measures.

Similarly, a failure attributable to inadequate osseointegration should be evaluated. If the correct implant systems are used, the negative outcome could be due to excessive heating of the bone during the surgical phase, incorrect prosthetic design leading to masticatory overload or an inadequate occlusal scheme, or alternatively, the patient's failure to stop or reduce smoking despite the dentist's recommendations.

In the case of implant loss due to incorrect positioning (such as contact with adjacent teeth, placement outside the ridge, or proximity between implants), the operator's responsibility for omitting preliminary steps (such as constructing of a surgical guide or bone grafts) is generally affirmed, except in rare cases.

These are just some of the potential causes of implant treatment failure, yet they highlight the challenging interpretation and evaluation of many cases of alleged professional liability, particularly when the failure occurs without a plausible technical explanation.[8]

In such cases, in the event of a dispute, it will be the healthcare provider's responsibility to demonstrate the correctness of their actions, including the assessment of potential contraindications, selection of suitable implants for the specific case, and adherence to healing times between the surgical procedure and prosthetic placement.

This last point introduces the medico-legal issue of immediate load implantology, which has emerged from ongoing efforts to reduce the operational time between the surgical placement of the implant and its prosthetic restoration. The goal is to provide earlier stabilization and functionalization of the prostheses, whether fixed or removable, as well as enhanced aesthetic comfort for the patient.

Current literature data have highlighted the efficacy of the immediate load technique, demonstrating high success rates. However, these outcomes are influenced by numerous factors related to the surgical phase, the host, the implant itself, and the occlusal situation.[9]

Surgical factors include primary stability and the surgical technique employed. Host-related factors encompass the quality and quantity of cortical and trabecular bone, the healing of the surgical wound, and the bone remodeling activity.

Primary stability is crucial, as any micromovements can influence cellular differentiation towards fibroblasts, leading to the formation of a fibrous capsule. This condition creates what is known as an 'indirect interface' between the bone and the implant, with connective tissue interposed.

As the interface expands, a 'peri-implant pocket' forms, leading to implant mobility and subsequent failure of the endosseous implants. Fibrous encapsulation can also occur due to surgical or thermal trauma during the site preparation phase.[9]

Host-related factors include the presence of metabolic disorders that may affect the healing of peri-implant tissues and the presence of dense, compact, and minimally porous bone, which has been shown to be crucial for the predictability of immediate load implantology. Additionally, patients with bruxism or parafunctional habits should be excluded from treatment, as these conditions are highly detrimental to osseointegration.

Such considerations are essential because, if treatment failure with potential adverse outcomes for the patient is attributable to a lack of osseointegration of the implant, and if the cause cannot be traced to general or specific risk factors related to the host, the operator's conduct must be analyzed. This involves evaluating the entire process, from the choice of treatment to the procedures implemented at each stage, including surgery, prosthetics, and ongoing monitoring to identify any subsequent complications.[2, 4, 9]

As previously stated, culpable conduct can be identified as negligent, imprudent, or incompetent behavior, which translates into a substantial alignment of the immediate-load technique with the issues previously discussed regarding failures of the traditional two-step technique.

A different consideration applies to specific fault, which is identified as the violation of established norms, laws, or regulations governing specific areas of healthcare practice.

In this context, forensic medicine tools used in evaluating professional responsibility rely on

guidelines, current scientific documentation relevant to the diagnostic and therapeutic moment in question (evidence-based medicine/dentistry), and reference frameworks on the usual course of the diagnosed and treated condition. The aim is to determine whether the professional's actions were guided by evidence at every stage or not. In the latter case, the investigation will focus on the reasons for deviating from established practices and the various therapeutic alternatives, while still respecting the autonomy of the healthcare professional.

Evidence-Based Dentistry, which is defined by the introduction of greater certainty in dentistry through a scientific approach based on randomized, controlled, and repeated clinical studies, aims to determine, based on diagnosis, which types of treatments are most likely to be beneficial to the patient in terms of the benefit-risk ratio.

From this, guidelines developed in various medical and dental disciplines, should serve as recommendations rather than rigid protocols. Therefore, a different diagnostic-therapeutic approach from these guidelines should not be synonymous with professional liability for the practitioner, provided that they bear the burden of demonstrating that they have acted appropriately.

The application of evidence-based dentistry (EBD) is realized through the conscious and rigorous use of the best available evidence to adopt the most appropriate solutions for the care of individual patients. This approach is based on a hierarchy of evidence levels, ranging from the highest level, including high-statistical-value randomized clinical trials and meta-analyses, to the fifth level, which encompasses case reports or anecdotal evidence.

Each of these levels of evidence corresponds proportionally to grades of recommendation.[9-11]

In the case of immediate-loading implantology, the medico-legal issue concerns the evidence supporting the choice of this technique, especially in response to any therapy failure that results in patient harm.

For different types of immediate-loading implant treatments, there are varying levels of scientific evidence based on the type of study conducted and the follow-up period. The immediate-loading overdenture on implants for edentulous mandibles is undoubtedly the most extensively studied therapy to date, demonstrating excellent success rates comparable to those of delayed loading (over 90%), as confirmed at 7-10 years.

Regarding single implants, although studies conducted so far have shown good results, these studies are often based on heterogeneous clinical case groups (post-extraction or edentulous sites) with relatively limited follow-up to date. This does not imply abstaining from practicing this method but rather adhering to established criteria to promote its success and, most importantly, providing adequate information to the patient, considering that one of the primary motivations for choosing this method is its aesthetic comfort.

Information and consent

The necessity of obtaining consent is grounded in Articles 13 and 32 of the Constitution and Article 39 of the Medical Code of Ethics. This fundamental and long-standing principle of informing the patient to obtain consent has led to increasingly rigorous legal, ethical, and medico-legal doctrines. Over the course of a few decades, it has become a cornerstone of the medical and surgical profession, closely linked to the principle of patient autonomy.[12]

The reference to evidence should not be seen as a shield for the practitioner, but rather as information that should be conveyed to the patient to ensure a balanced sharing of decisions, taking into account the patient's needs and expectations. The failure to meet these expectations often serves as the starting point in medico-legal disputes. Therefore, it is crucial to establish a care contract with the patient, based on the most comprehensive information possible. This is because the obligation of the dentist is closely tied to what is presented and thus accepted by the patient.

Undoubtedly, practical difficulties in the duty of informing the patient cannot be disregarded, particularly concerning the patient's age, cultural background, emotional state, and mental competence.

It is therefore essential to discuss with the patient, tailoring the information as much as possible to their specific needs and clarifying the type

of proposed treatment, its duration, the operator's experience with the indicated technique or solution, the available therapeutic alternatives, potential discomforts, achievable outcomes, risks, and foreseeable complications of the therapy (and possibly of not receiving therapy), the quality of the various materials applicable in each case, and the behavior to be followed at different stages and at the end of the treatment.[13]

In the specific case of immediate loading, where conditions permit its execution, this procedure should be explained to the patient, emphasizing that studies with single implants have shown positive results but with relatively limited follow-up, compared to the traditional delayed loading technique, which has a 98% success rate and has now been applied and monitored for thirty years.

Therefore, it would currently be advisable to perform immediate loading only upon the patient's explicit request, leaving the decision to them after providing appropriate information, and ensuring they have precise factual elements, including those related to the prognosis.

Regarding the acquisition of consent, there is currently no legal obligation for written documentation of consent. However, given that these treatments are never urgent and extend over time, it is advisable to request and obtain written formalization. This written form represents the best means for the legitimate protection of the dentist, facilitating the burden of proof regarding the provision of information in case of legal disputes.

This need has led to the widespread use of standard forms in many dental practices, which, while documenting consent, are often overly generic and resemble waiver forms more than informative documents. These forms typically lack specific references to the information provided and the characteristics of the intervention, which undermines their validity.

It would therefore be advisable to use more specific forms, detailing the peculiarities of the planned treatment, and particularly referencing the achievable results and potential complications, especially in the case of immediate-loading implantology. Additionally, as previously mentioned, these forms should address the possibility of treatment failure, even with a correctly performed procedure.

Finally, it is important to emphasize the need for strict adherence to pre- and post-surgical instructions, as well as the necessity for regular follow-up visits and both professional and home oral hygiene measures.

It is important to clarify that proper information and consent do not absolve the practitioner of responsibility in the event of errors. It is also important to emphasize that, despite the adoption of measures of diligence, expertise, and caution, it is not possible to completely rule out the occurrence of an adverse event. Our information sheet and consent form for osseointegrated implant surgery is provided in Supplementary Digital Material 1 (Supplementary File 1).

Medical record

All patient-related information and the step-by-step progression of the therapeutic process should be appropriately recorded, either through paper or electronic documentation.

The need to compile detailed medical records documenting the entire therapeutic process has increasingly grown, both to adequately record all patient-related data (including anamnesis, clinical, and instrumental information) to provide higher-quality care, and for medico-legal purposes to substantiate clinical circumstances that might otherwise be unproven, particularly in the event of legal disputes.

Therefore, the importance of meticulous record-keeping is evident, even though, in the context of private practice, medical records do not hold the status of an official document, unlike in public institutions.

Officially, there is no legal requirement mandating the creation and storage of medical records for private practices and outpatient clinics. Unfortunately, this often results in insufficient data being recorded, and in some cases, a complete lack of documentation.

Aspects that may not seem immediately relevant to daily practice, such as thorough medical history, archiving of radiographs and plaster models, and maintaining a clinical diary, are sometimes overlooked. However, these elements

become critically important in the event of a legal dispute.

Moreover, there is currently a judicial trend that views the meticulous documentation and preservation of patient records as evidence of the professional's diligence. Conversely, failing to adhere to these practices is considered an act of negligence, potentially impacting the assessment of any potential liability.

To meet the requirements of completeness and accuracy, the patient record should be structured approximately as follows:

- date of entry;
- patient's name, personal details, and address;
- general medical history;
- dental history;
- initial dental formula;
- orthopantomogram and intraoral radiographs;
- plaster models (with traceability references);
- diagnosis and proposed treatment plan;
- financial plan accepted by the patient;
- information sheet regarding the therapy to be undertaken;
- informed consent;
- clinical diary with chronological records of various appointments;
- any modifications to the proposed treatment plan;
- schedule for periodic check-ups and professional oral hygiene sessions;
- home hygiene and behavioral instructions.

To enhance the evidentiary value of the clinical record, it would be beneficial to have the patient initial each entry at the end of every session, particularly for complex treatments requiring multiple appointments, such as implant prosthetics.

Additionally, missed follow-up appointments or hygiene sessions and any refusal to continue therapy should be documented to prevent unjust attributions of responsibility.

Despite the limitations due to the lack of specific regulations, and aiming to align with practices in the public sector, from a legal and ethical standpoint, clinical documentation, given the right to protect one's own health, belongs to the patient. Therefore, if the patient requests it, the dentist has the duty to provide it, including radiographs.

In such cases, it would still be prudent for the dentist to retain a copy in their records for precautionary reasons, after also obtaining a signed acknowledgment of receipt from the patient.

Finally, it is important to note that, in light of the increasing use of digital supports, current legislation in our country recognizes the validity of radiographic images in electronic format and digital databases.

In conclusion, in cases of litigation, well-prepared and properly maintained clinical documentation serves as an invaluable source for determining potential professional liability. It allows for a thorough review of the entire treatment process, from diagnosis to conclusion, to verify whether the dentist employed all appropriate measures for the specific case. This documentation can also be equally valuable for the patient, proving or disproving adherence to periodic check-ups and prescribed guidelines.[14]

A final summary reflection can be made regarding the importance of ensuring that a performance adheres as closely as possible to the fundamental basic preparation, guidelines, and evidence-based medicine, with allowances for the limitations and exceptions applicable to individual specific cases, always respecting and prioritizing the patient's interests.[15]

In this regard, it is important to emphasize the previously mentioned need for mutual understanding, involving comprehensive information about the various therapeutic options. This includes, particularly with respect to immediate-load implantology, mentioning the potential limitations of the methodology, which may also involve insufficient experience on the part of the operator.[16]

In conclusion, it is crucial to highlight the need for a well-organized practice, especially for more complex cases. This should include proper documentation archiving, ongoing patient monitoring, and, in cases involving multiple practitioners, collaborative evaluation and constant communication among the professionals involved.[17]

Finally, in the event of a potential conflict, the best approach would be to avoid rigidly adhering to one's own "certainties." Instead, it is advisable to address any requests for clarification from the patient and facilitate, where possible, the resolution of misunderstandings.[18]

The following is an example of an informational sheet on implant treatment (with reference to immediate loading). However, it should be noted that any pre-printed form used should be supplemented with specific references to the individual patient.[19]

In particular, it is important to highlight the necessity of preliminary treatments, such as sinus lift, bone grafts, etc.; and the presence of anatomical features that may affect the aesthetic outcome, such as gingival thickness and quality; the presence of pre-existing dental conditions that may impact the therapy, as well as specific patient needs that drive the choice of a particular therapeutic solution (such as immediate loading due to aesthetic requirements) rather than another option.[20]

It is indeed important that the information be as comprehensive as possible regarding the general aspects of the proposed treatment, but also tailored to each specific case.[21]

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Conflicts of interest
The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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Conceptualization: Michele A. Karaboue, Giorgia V. Lacasella. Methodology: Eleonora Lo Muzio. Software: Karidia Karaboue. Validation: Maria E. Bizzoca and Swapnil Saini. Formal analysis: Francesco Pettini. Investigation: Michele Di Cosola. Resources: Michele Covelli. Data curation: Lynn Almasri. Writing—original draft preparation, Michele A. Karaboue. Writing—review and editing, Maria E. Bizzoca, and Giorgia V. Lacasella. Visualization: Karidia Karaboue. Supervision: Lynn Almasri. All authors have read and agreed to the published version of the manuscript.

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