

## Research Article

# Gastroscope Yield in the Young: Comprehensive Assessment of Endoscopic and Histologic Findings—A Comparative Study

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**Background.** The escalating utilization of gastroscopy in young individuals necessitates an in-depth examination of its diagnostic yield and outcomes in this population. This study aims to investigate and compare various aspects of gastroscopy between young and older adults, shedding light on age-related differences in indications, endoscopic findings, histologic outcomes, and clinically significant findings (CSFs). **Methods.** A retrospective, large cohort study spanning five years, focused on consecutive patients undergoing gastroscopy. We analyzed age subgroups, specifically categorizing patients into those aged 30 and below, 30–39, 40–49, and a control group aged 50 and above. The investigation aimed to compare various aspects of gastroscopy outcomes among these distinct age categories. Indication-based analyses were conducted to assess the yield and outcomes in these subgroups, focusing on CSFs and the number needed to investigate (NNTI). **Results.** A total of 1313 young patients aged 16–49 and 3396 controls aged 50 and above were included. Among the young patients, unspecified epigastric pain and dyspepsia emerged as a prevalent indication, accounting for 41.5% of cases. Endoscopic findings revealed a significantly higher diagnosis rate of gastritis than controls (48.2% vs. 35.7%;  $p < 0.001$ ). Histologic analysis demonstrated a substantially elevated rate of *H. pylori*-associated gastritis in the young (41.1% vs. 29%;  $p < 0.001$ ). Notably, although significantly lower than older controls, precancerous lesions were detected in 7.5% of young patients. CSFs' diagnosis rate displayed a clear age-dependent increase. Particularly, gastroscopy for upper gastrointestinal bleeding and iron deficiency anemia were associated with higher CSF rates across all young-age subgroups. In multivariate analysis, age and indications of upper gastrointestinal bleeding and iron deficiency anemia were predictors of CSFs' detection in young patients. **Conclusion.** This study comprehensively delineates various facets of gastroscopy in the young population, elucidating age and indication-specific patterns in endoscopic and histologic findings, and clinically significant outcomes.

## 1. Introduction

Symptoms related to upper gastrointestinal conditions are widely encountered in general practice, responsible for substantial healthcare costs, and significantly affecting the quality of life [1, 2]. Among these symptoms, dyspepsia and heartburn account for sizeable outpatient visits to general

practitioners and primary care centers, constituting over a quarter of all gastroenterology appointments [3, 4]. Gastroscopy is, unquestionably, the most accurate diagnostic method for most conditions associated with upper GI symptoms. However, endoscopy is invasive and involves discomfort, inconvenience, and cost [5]. Previous attempts to identify patients most likely to benefit from endoscopy

have produced variable results, particularly among younger patients [6]. Multiple studies have reported low yields of gastroscopy when evaluating patients with dyspepsia or reflux-related symptoms who are less than 50 years old and otherwise healthy [7, 8]. These findings have led society guidelines to recommend avoiding routine gastroscopy in dyspeptic patients under 60, with the consideration of endoscopy in younger patients with dyspepsia on a case-by-case basis, without automatic consideration due to alarm features [9, 10].

Despite these recommendations, several observations have documented poor adherence to these guidelines, with gastroscopy still being widely performed in young adults, often without significant findings [11, 12]. Importantly, data regarding the use and outcome of gastroscopy for young individuals under 50 years presenting with upper GI symptoms other than dyspepsia are scarce and were not evaluated in a large-scale study [13]. Therefore, through a focused analysis of indications, endoscopic findings, and histologic outcomes, we aimed to provide valuable insights into the evolving diagnostic landscape in the young patient demographic, with the overarching objective of elucidating the yield and outcomes of gastroscopy and contributing to the development of tailored diagnostic approaches that optimize clinical effectiveness and resource allocation.

## 2. Materials and Methods

A retrospective, large cohort study was conducted by reviewing electronic files of consecutive patients who underwent gastroscopy over a 5-year period (2015–2020) within the gastroenterology department at the Hillel Yaffe Medical Center, a university-affiliated hospital in Israel. All patients' data were collected from our department's electronic record system. Inclusion criteria encompassed patients with complete documentation of clinical, endoscopic, and histologic findings. Patients under the age of 18 years, those with past gastric or esophageal surgery, and those with a personal history of upper GI malignancy were excluded.

Full demographic data of patients upon admission into the endoscopy unit were recorded based on identity details and the national database. Relevant clinical and endoscopic findings, including procedures' indications, clinical presentation, procedural setting and timing, sedation regimen, and provider, were documented. The major extracted measures of the outcome included the presence and grade of reflux esophagitis (classified as A–D based on the Los Angeles scale), Barrett's esophagus presence and maximal length (based on endoscopic and histologic evidence), esophageal malignancy diagnosis (pathologically confirmed), and location. Moreover, peptic ulcer disease description, location, and severity (gastric and duodenal), gastric vascular lesions, and gastric malignancy were documented. In addition, the endoscopic interventions during the endoscopy procedure and pathology results from biopsies were tracked. Based on the patients' age at presentation, a young patient group (50 or below) and a control group of older adults (above 50 years) were created.

The clinical, procedural, endoscopic, and pathological outcomes were compared between both groups. Multivariate analysis was performed to identify predictors for upper GI malignancy and CSFs, defined as the presence of severe reflux esophagitis (class C–D), Barrett's esophagus, esophageal malignancy, severe peptic ulcer disease, large (>1 cm) gastric polyps, severe angioectasia, and/or gastric or duodenal malignancy.

*2.1. Statistical Analysis.* Continuous parameters were presented as mean  $\pm$  standard deviations, and categorical parameters were expressed using frequencies and percentages. Differences within and between the younger age and the control groups were compared by the *t*-test in quantitative parameters and the Fisher's exact test in the categorical parameters. Multivariate analysis by logistic regression was used to identify predictors of CSFs. SPSS version 25 was used for the statistical analysis, with a  $p < 0.05$  considered significant.

## 3. Results

*3.1. Demographic and Clinical Characteristics of Study Participants.* Table 1 presents the demographic and clinical characteristics of the study participants stratified by age groups. A total of 1313 patients aged 16–49 and 3396 patients aged 50 and above were included in the final analysis.

The mean age of the younger group (16–49 years) was  $34.7 \pm 10.4$  years, while the older group (50 years and above) had a mean age of  $67.01 \pm 10.3$  years. Gender distribution revealed that 46% of patients in the younger group were male, compared to 47% in the older group ( $p = 0.52$ ). Ethnic affiliation exhibited notable differences between the groups. Despite the fact that the majority of patients in both groups were Jewish, reflecting the background distribution in our population, 71.5% of patients in the younger group were identified as Jewish, while 85% of patients in the older group were of the same religious affiliation ( $p < 0.001$ ).

Gastroscopy indications demonstrated substantial variations between the two age groups. Notably, anemia was a more common indication in the older group, with 18.3% of patients presenting with this symptom, compared to 8.8% in the younger group ( $p < 0.001$ ). Conversely, epigastric pain was more prevalent among younger patients, with 41.5% reporting this symptom, in contrast to 25.5% in the older group ( $p < 0.001$ ). Notably, vomiting, reflux-related symptoms, weight loss, and several other indications were not significantly different between the two age groups.

*3.2. Endoscopic Findings.* Table 2 outlines the diagnoses obtained through gastroscopy in the two age groups. Notable differences emerged in the occurrence of gastric ulcers, gastric polyps, vascular lesions, and hiatus hernias. A total of 139 patients (10.6%) in the younger group were diagnosed with hiatus hernia, while this condition was observed in 714 patients (21.0%) in the older group, reflecting a statistically significant difference ( $p < 0.001$ ). Gastric ulcers were present in 0.9% of younger patients compared to 2.2% of older

TABLE 1: Baseline characteristics of both groups.

Characteristic	Age 16–49 <i>n</i> (%) <i>N</i> = 1313	Age ≥ 50 <i>n</i> (%) <i>N</i> = 3396	<i>P</i> value
Age (years)	34.7 ± 10.4	67.01 ± 10.3	<0.001
Sex (male)	608 (46)	1609 (47)	0.52
Ethnicity (Jews)	939 (71.5)	2877 (85)	<0.001
<i>Gastroscopy indication</i>			
Anemia	116 (8.8)	323 (18.3)	<0.001
Dyspepsia	177 (13.5)	398 (11.7)	0.10
Heartburn	108 (8.2)	303 (8.9)	0.49
Vomit/nausea	82 (6.2)	170 (5.0)	0.097
Upper gastrointestinal bleeding	27 (2.1)	160 (4.7)	<0.001
Dysphagia	23 (1.8)	141 (4.2)	<0.001
Weight loss	36 (2.7)	192 (5.7)	<0.001
Epigastric pain	545 (41.5)	865 (25.5)	<0.001
Positive FOBT	3 (0.2)	105 (3.1)	<0.001
Imaging findings	13 (1.0)	87 (2.6)	<0.001
Low B12	16 (1.2)	24 (0.7)	0.11
Diarrhea	76 (5.8)	73 (2.1)	<0.001
Other	149 (11.3)	335 (9.9)	0.13

TABLE 2: Endoscopic findings of both groups.

Gastroscopy diagnosis	Age 16–49 <i>n</i> (%) <i>N</i> = 1313	Age ≥ 50 <i>n</i> (%) <i>N</i> = 3396	<i>P</i> value
Hiatus hernia	139 (10.6)	714 (21.0)	<0.001
Gastritis	633 (48%)	1212 (35.7)	<0.001
Duodenitis	204 (15.5)	553 (16.3)	0.56
Reflux esophagitis	83 (6.3)	217 (6.4)	1.00
Barrett's esophagus	17 (1.3)	58 (1.7)	0.36
Infectious/other esophagitis	17 (1.3)	53 (1.6)	0.59
Esophageal varices	6 (0.5)	32 (0.9)	0.10
Esophageal carcinoma	0 (0.0)	6 (0.2)	0.19
Gastric ulcer	12 (0.9)	74 (2.2)	0.003
Gastric carcinoma	1 (0.1)	8 (0.2)	0.74
Duodenal ulcer	15 (1.1)	59 (1.7)	0.15
Gastric polyps	41 (3.1)	319 (9.4)	<0.001
Vascular lesion	1 (0.1)	29 (0.9)	0.002
Submucosal lesion	8 (0.6)	30 (0.9)	0.47
Stomach postsurgical	23 (1.8)	56 (1.6)	0.80
Other	20 (1.5)	71 (2.1)	0.24

patients ( $p < 0.003$ ). Gastric polyps were observed in 3.1% of younger patients and 9.4% of older patients ( $p < 0.001$ ). Vascular lesions were present in 0.07% of younger patients and 0.9% of older patients ( $p < 0.002$ ).

In contrast, diagnosis of gastritis was significantly higher in the young-age group (48.2% vs. 35.7%;  $p < 0.001$ ) than in older controls.

No statistically significant differences were found in the diagnoses of duodenitis, duodenal ulcer, reflux esophagitis, Barrett's esophagus, candida or other unspecified esophagitis, esophageal varices, and gastric submucosal lesions. A trend of increased diagnosis rate of esophageal and gastric carcinoma was documented but did not reach statistical significance due to the very low prevalence of upper gastrointestinal cancers in our cohort.

However, notable differences emerged in the occurrence of gastric ulcers, gastric polyps, vascular lesions, and hiatus hernias. Gastric ulcers were present in 0.9% of younger patients compared to 2.2% of older patients ( $p < 0.003$ ).

Gastric polyps were observed in 3.1% of younger patients and 9.4% of older patients ( $p < 0.001$ ). Vascular lesions were present in 0.07% of younger patients and 0.9% of older patients ( $p < 0.002$ ).

**3.3. Major Pathological Findings.** The major pathology findings of biopsy specimens included *H. pylori*-associated gastritis, evident in more than 40% of young patients, significantly higher than in older controls (41.1% vs. 29%,  $p < 0.001$ ). Almost one-third of patients in both groups had chronic unspecified gastritis (Table 3). However, the rate of precancerous lesions was significantly higher in the old groups (20.7% vs. 7.5%,  $p < 0.001$ ).

**3.4. CSFs and NNTI in Young-Age Subgroups and Controls.** The diagnosis rate of CSF and the corresponding NNTI in different age groups showed a distinct trend (Figure 1). Among patients aged 30 and below, the CSF percentage was

TABLE 3: Major pathology findings for both groups.

Histologic findings	Age 16–49 <i>n</i> (%) <i>N</i> = 1313	Age ≥ 50 <i>n</i> (%) <i>N</i> = 3396	<i>P</i> value
<i>H. pylori</i> -positive	539 (41.1)	984 (29.0)	<0.001
Chronic gastritis unspecified	378 (28.8)	1154 (34.0)	<0.001
Gastric atrophy	11 (0.8)	95 (2.8)	<0.001
Gastric intestinal metaplasia	89 (6.8)	649 (19.1)	<0.001
Dysplasia	0 (0.0)	14 (0.4)	0.015
Precancerous lesions overall	99 (7.5)	703 (20.7)	<0.001

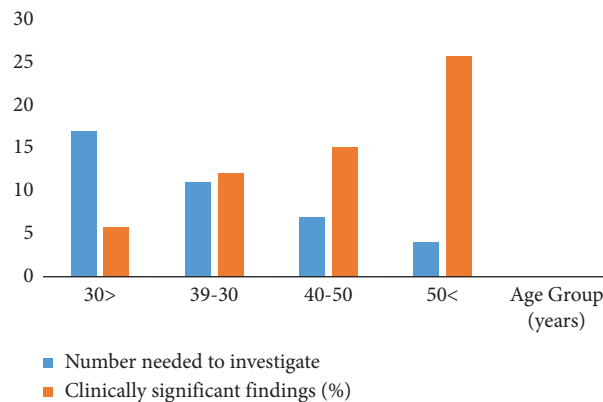


FIGURE 1: Clinically significant findings and the number needed to investigate trends throughout age groups.

notably low at 5.8%, and the NNTI was relatively high at 17, signifying the need for approximately 17 gastroscopic procedures to identify one case of clinically significant findings in this younger age group. As age increased to the 31–39 and 40–50 age groups, the CSF percentages gradually grew to 12.1% and 15.2%, respectively. Simultaneously, the NNTI decreased to 11 and 7 in these respective age groups. The trend continued in the 50 and above age group, where the CSF percentage was the highest at 25.8%, which is significantly higher than all other young-age groups ( $p < 0.01$ ) and the NNTI was the lowest at 4.

**3.5. Indication-Based Analysis of CSF in Young Patients and Controls.** The diagnosis rate of CSFs for each young-age subgroup and older controls is provided in Figure 2. Overall, a trend of increased detection of CSF was noted with age throughout all indications. Notably, performing gastroscopy for the investigation of upper gastrointestinal bleeding was associated with the highest rate of CSF diagnosis (27.3%, 35%, and 26.7% vs. 42.5%;  $P^{1,2,3} < 0.01$ ) in younger patients below 30, 30–39 years, 40–49 years, and control patients above 50, respectively. Furthermore, indications of iron deficiency anemia and dyspepsia were associated with the highest yield of endoscopic evaluation in terms of CSF detection (Figure 2).

**3.6. Predictors of CSF in Multivariate Analysis.** The multivariate analysis revealed that the male sex (odds ratio = 1.41;  $p < 0.001$  and 95% CI = 1.22–1.63), and indications of upper GI bleeding (odds ratio = 2.15;  $p < 0.001$  and 95% CI = 1.57–2.94)

and iron deficiency anemia (odds ratio = 1.61;  $p < 0.001$  and 95% CI = 1.42–1.85) were associated with increased risk of CSF. All young-age groups were associated with reduced risk of CSF: <30 years (OR = 0.19;  $p < 0.001$ ), 30–39 (OR = 0.42;  $p < 0.001$ ), and 40–49 (OR = 0.52;  $p < 0.001$ ).

#### 4. Discussion

The escalating referral of young patients for gastroscopy, constituting more than one-third of the procedures in our cohort, reflects the increasing prevalence of gastroscopy utilization in young patients [14]. This trend underscores the importance of understanding the unique clinical characteristics and outcomes associated with gastroscopy in this demographic.

In exploring the major indications for gastroscopy in the young, dyspepsia and other unspecified epigastric pain emerge as predominant symptoms, constituting a substantial proportion of cases. This prevalence surpasses that observed in older adults, highlighting the distinctive challenges in managing upper gastrointestinal symptoms in the younger demographic. In this regard, the observation that more than 40% of young patients exhibit *Helicobacter pylori* (HP) gastritis raises important considerations. This finding suggests a potential deviation from established guidelines recommending endoscopy primarily for individuals above 50–60 years or those with alarm features [15]. The incorporation of noninvasive HP testing, such as breath tests, could potentially mitigate the need for gastroscopy in a substantial number of cases, thereby reducing procedural burden and associated healthcare costs. Taken together with findings presented by Räsänen and van Nieuwenhoven [12]

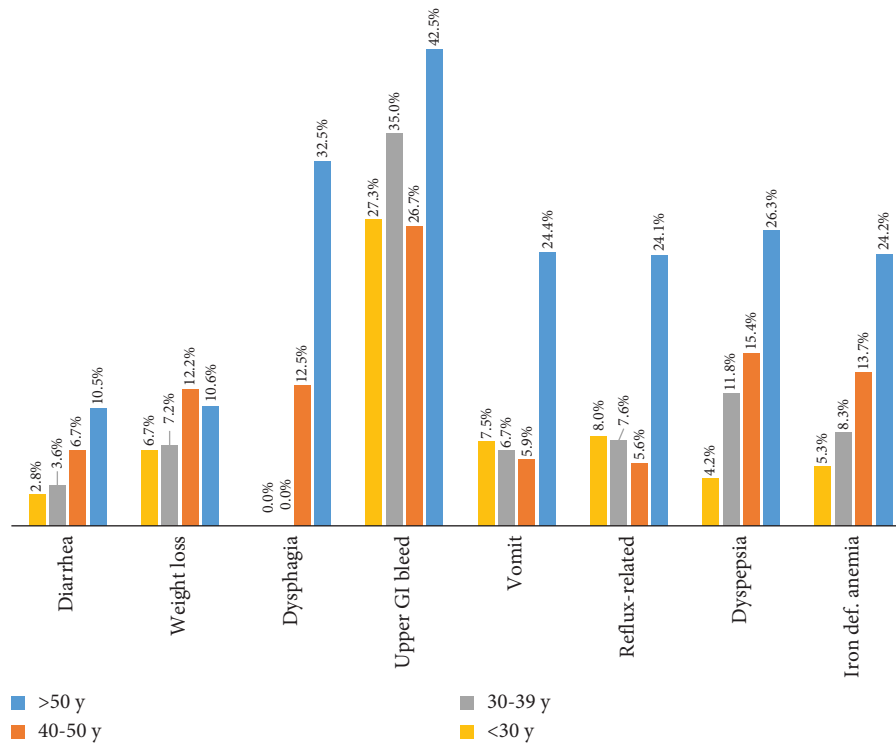


FIGURE 2: Clinically significant findings' diagnosis rate as per indication throughout the age groups.

indicating upper endoscopy performance based on primary healthcare referrals demonstrated almost exclusively benign pathology, this underscores the imperative need to foster enhanced cooperation between primary care providers and gastroenterologists while concurrently emphasizing the necessity to heighten awareness among primary care providers regarding the management and workup of dyspeptic patients.

Noteworthy, although medical literature has mainly focused, addressed, and discussed dyspepsia as a major indication for gastroscopy in this young population [16], we provided detailed referral indications for this age group, highlighting the diverse clinical presentations and the referral trends. The abovementioned conclusions are also relevant to other common referral indications in young patients, where proper management and workup of patients, such as optimizing proton pump inhibitor (PPI) use and addressing lifestyle changes for those with reflux-related symptoms, meticulously reviewing other causes of anemia, particularly in young female patients, and conducting a more comprehensive assessment of weight loss in the preendoscopy evaluation, have the potential to lower the need for upper endoscopic evaluation [12].

The analysis of endoscopic findings showed that a noteworthy disparity in the distribution of gastrointestinal pathologies emerges between young and older adults. The high rates of gastritis, duodenitis, and duodenal ulcers among young patients may indicate a considerable burden of peptic ulcer disease in this age group, possibly due to the high rate of HP documented in this age group. Conversely, older adults exhibited elevated rates of precancerous lesions,

polyps, and possibly neoplasms, signifying a shift in the spectrum of gastrointestinal disorders with advancing age. Moreover, a higher rate of gastric ulcers was documented in older control patients than in younger patients. These findings are similar to those reported by Groenen et al. [17], documenting increasing nonmalignant gastric ulcers with age, possibly due to comorbidities, polypharmacy, and increased use and effect of NSAIDs.

The age-stratified analysis of CSF delineates a progressive increase with advancing age. Higher CSF rates in older adults illuminate the age-associated rise in the prevalence of pathological conditions necessitating endoscopic evaluation. Indeed, studies have demonstrated a trend of increased GI pathology among age through the upper and lower gastrointestinal tracts [18]. Notably, this escalation in CSF rates corresponds to a concurrent decrease in the NNTI, underscoring the heightened diagnostic yield in older age groups. It is crucial to acknowledge that while our study provides age-related NNTI, it was not specifically designed to establish age cut-offs for endoscopic investigations across various indications, but may provide a basis for other studies to assess age-related yield and cut-offs, particularly as our study was unique with the inclusion of multiple age subgroups and procedures' indication, as age cut-offs previously focused on dyspepsia only and were not relevant to other indications [19]. Furthermore, our study, focusing on CSF, reveals that the NNTI increases significantly when considering upper gastrointestinal cancer rates, emphasizing the need for a judicious approach. Thus, due to the very low prevalence of upper GI malignancies, similar to other several western populations [20], we focused the discussion on CSF,

but we should highlight that if the primary aim or point of discussion is upper GI cancer, the yield of gastroscopy in the young will be very low and age-cutoff should be raised. Taken together, these findings align with the recent guidelines advocating for an increase in the age cutoff for performing gastroscopy, given the relatively low prevalence of upper gastrointestinal cancers in younger age groups, but the analysis should be population-dependent as the risk of upper GI cancer varies [21, 22].

Beyond age-related analysis, we performed an in-depth indication-based analysis, uncovering distinctive patterns in the yield of CSF. Notably, indications such as upper gastrointestinal bleeding and iron deficiency anemia, both considered as alarm features, were associated with the highest yield of CSF detection, underscoring the diagnostic relevance of these symptoms. Conversely, indications such as reflux-related symptoms, vomiting, diarrhea, and weight loss (although considered an alarming symptom) exhibited a comparatively lower yield. This nuanced indication-based analysis emphasizes that not only age but also the specific clinical presentation should be considered when referring patients for gastroscopy. It is noteworthy that our exploration of indication-based outcomes in this age group represents a novel contribution to the literature. We could not find a dedicated study of performing multiple indication-based analyses of gastroscopic outcomes, particularly in the younger demographic. Although further confirmation is needed, our findings may aid in guiding clinicians to tailor their approach based further on the presenting symptoms, thereby optimizing the diagnostic yield and resource utilization in this specific patient population, and suggest that this issue warrants further evaluation in future studies.

One noteworthy finding of the current study, when reviewing pathology reports, was the identification of precancerous lesions in 7.5% of young patients, underscoring the imperative for further investigation. These findings hint at a complex interplay of factors, potentially linked to HP infection or chronic gastritis. Despite the increasing awareness of these conditions, we could not find studies that address this particular concern in young patients. Future research endeavors should focus on elucidating clinical and endoscopic predictors for precancerous lesions in young patients, facilitating targeted interventions and long-term surveillance strategies to mitigate the risk of progression to malignancy [23].

The strengths of the current study lie in the inclusion of a large cohort with comprehensive clinical, endoscopic, and pathological data. The age- and indication-based analyses provide valuable insights into the intricate dynamics of gastroscopy utilization in the young patient population. However, inherent limitations, such as the retrospective, single-center nature of the study, should be acknowledged. In addition, it is important to note that other potential confounders, such as BMI, PPI use, NSAIDs, and family history, were not included in the dataset, and their absence may impact the interpretation of outcomes.

In conclusion, our study unveils the increasing prevalence of gastroscopy in young patients, illustrating

a consistent increase in CSFs with age and identifying indications associated with elevated CSFs. The findings underscore the need for tailored diagnostic strategies based on age and indication. Future multicenter studies could enhance generalizability, providing a deeper understanding of gastroenterological trends and offering practical guidance for endoscopy utilization while exploring strategies to reduce unnecessary procedures, confirming and expanding upon our current findings.

## Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

## Authors' Contributions

All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Fadi Abu Baker, Amir Mari, Randa Taher, Oren Gal, Dorin Nicola, Majeed Zahalka, and Abdel-Rauf Zeina. The first draft of the manuscript was written by Fadi Abu Baker and Abdel-Rauf Zeina, and all authors commented on the previous versions of the manuscript. All authors read and approved the final version of the manuscript.

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