

Children with diseases of the upper gastrointestinal tract are more likely to develop feeding problems

Katerina Sdravou^a, Elpida Emmanouilidou-Fotoulaki^a, Maria-Rafaela Mitakidou^a, Anastasia Printza^b, Athanasios Evangeliou^a, Maria Fotoulaki^a

School of Medicine, Aristotle University of Thessaloniki, General Hospital "Papageorgiou"; School of Health Sciences, Aristotle University of Thessaloniki, Thessaloniki, Greece

Abstract

Feeding problems may give rise to a number of adverse effects with organic, psychological, developmental and social impact. Specific medical conditions, especially diseases of the gastrointestinal system, are known to be associated with feeding problems. We searched databases, including MEDLINE and the Cochrane Library, for papers published in English from 1990 to March 2018. Keywords included "gastrointestinal diseases", "gastroesophageal reflux disease", "eosinophilic esophagitis", "food allergy", "children", "infants", and "feeding problems". We concluded that children with diseases of the upper gastrointestinal tract, especially those with gastroesophageal reflux disease and eosinophilic esophagitis, are more likely to develop feeding problems. However, further epidemiological studies are needed to determine the prevalence and the specific characteristics of feeding problems in children with certain upper gastrointestinal diseases, as well as the exact causal relationship between them.

Keywords Feeding problems, gastrointestinal diseases, gastroesophageal reflux disease, food allergy, eosinophilic esophagitis

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Introduction

Feeding is an intricate process that requires the biological regulation of appetite and satiety, the availability of food, the transferring of food into the mouth, the preparation of bolus in the mouth, swallowing, digestion, and evacuation. It takes place in a socio-cultural context by which it is significantly affected [1]. A large number of biological, psychological, socio-cultural and environmental factors interact, jointly shaping and interfering in this process of development [2,3].

The elimination or deregulation of any of these factors entails a variety of problems that can occur in a wide range of activities

related to feeding [1]. The manifestation of feeding problems includes a diversity of symptoms: for example, complete or partial food refusal, food selectivity, dietary restriction, adherence to behavior that does not correspond to the stage of development, tube feeding dependence, reduced appetite, lack of self-sufficiency in feeding, and dysfunctional behaviors during meals [4,5]. These problems may be accompanied by swallowing disorders [6,7].

Feeding problems are associated with a number of negative effects at the organic, psychological, developmental, and social levels. Even when they do not affect nourishment and growth, they are capable of significantly degrading the quality of life of the child and the family and may result in a negative relationship between parents and children [8]. Although the majority of children present no difficulty in feeding and growing, feeding disorders in early childhood are frequent. Feeding problems are estimated to occur in 25-35% of children with normal growth, whereas in children with growth disorders this may reach as high as 85% [9]. However, feeding problems comprise a heterogeneous group and the lack of a clear definition should be taken into consideration when estimating their prevalence [10]. This makes it difficult to identify, prevent and detect feeding disorders early in order to treat them effectively. The widely accepted opinion is that organic, environmental and behavioral factors interact and result in feeding problems [11]. Certain clinical studies point out the fact that specific medical conditions, especially diseases of the gastrointestinal

^a4th Department of Pediatrics, School of Medicine, Aristotle University of Thessaloniki, General Hospital "Papageorgiou" (Katerina Sdravou, Elpida Emmanouilidou-Fotoulaki, Maria-Rafaela Mitakidou, Athanasios Evangeliou, Maria Fotoulaki); ^b1st Otolaryngology Department, Medical Department, School of Health Sciences, Aristotle University of Thessaloniki (Anastasia Printza), Thessaloniki, Greece

Correspondence to: Katerina Sdravou, SLT, MSc, SpeechLab, Adrianoupoleos 55, 55133, Thessaloniki, Greece, e-mail: sdravouk@tcd.ie

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system, are linked with feeding problems [12-39]. The aim of this review was to examine whether children with upper gastrointestinal diseases are more likely to present with feeding problems. This article provides a brief overview of the association between feeding problems and upper gastrointestinal diseases. Based on the findings of this review, gastroesophageal reflux disease (GERD) and eosinophilic esophagitis are the leading organic causes of feeding problems in children with typical development [15-23,35-39]. Food allergy and intestinal motility disorders are also associated with feeding problems, but have not been the subject of systematic controlled studies [18,26-34,36].

Materials and methods

We conducted a review of articles published on pediatric feeding disorders from 1990 to March 2018. Electronic databases were searched, including MEDLINE, EMBASE, Cochrane Library and Google Scholar. The literature review was performed using the following MeSH terms: “gastrointestinal diseases”, “gastroesophageal reflux disease”, “eosinophilic esophagitis”, “food allergy”, “children”, “infants” and “feeding problems”. Initially 650 studies were retrieved. Studies of feeding disorders due to other etiologies, such as diseases of the lower gastrointestinal tract, neurological disorders, prematurity, autism, sensory problems and environmental issues, were excluded. Only studies published in English were included. Finally, 20 studies of feeding disorders in children with diseases of the upper gastrointestinal tract were selected. A flow chart illustrating the study selection process is shown in Fig. 1. Table 1 summarizes the studies evaluated.

Results

Feeding problems in children with GERD

Clinical manifestations of GERD in children include recurrent regurgitation, vomiting, abdominal pain, heartburn, poor weight gain, and irritability. When GERD symptoms remain untreated they are associated with a decrease in quality of life, for both the children and their families, and may lead to complications, such as reflux esophagitis, failure to thrive, esophageal stricture and Barrett’s esophagus [12,13]. GERD may also cause decreased laryngopharyngeal sensitivity, laryngitis, sinusitis, increased frequency of silent aspiration, pulmonary infections, bronchiectasis and apnea, as well as asthma [14]. Furthermore, GERD is the disease most commonly linked with feeding pain; as a result, the biological need for feeding is overcome by the desire to avoid the annoying stimulus. Aversion is more intense when connected with oropharyngeal dysphagia and aspiration incidents [13].

A clinical study of 201 children with feeding problems verified that 76% of them had a certain medical disorder, with the majority (41%) being GERD patients [15]. In a



Figure 1 Study flow diagram

sample of 72 feeding tube-dependent children, organic causes were dominant: 83% of the sample had a diagnosis of oropharyngeal and gastrointestinal abnormalities and 64% had a diagnosis of cardiac, pulmonary, neurological or genetic disease [16]. A review of 38 intervention studies in the literature demonstrated that 212 of 218 participants with feeding problems who received treatment suffered a specific medical condition. Among these, 55% were diagnosed with a gastrointestinal disorder, mainly GERD [17]. Another study of childhood feeding problems demonstrated that the vast majority of the children (340 of 349) had a certain organic disorder and most commonly GERD (51%). With regard to the type of feeding problem, 34% had food refusal, 21% selectivity by food type, 26% selectivity by food texture, 44% oral motor disorders, and 23% dysphagia. The frequency and severity of the feeding problem, and especially of food refusal, were greater in children with GERD than in those with other organic disorders. Specifically, 69% of the children who had food refusal also had GERD [18].

According to another study, children with GERD present with food refusal and selectivity, which persists after the treatment of the organic cause. Additionally, it is possible to develop oral and tactile hypersensitivity that aggravates the transition to solid food and hinders the acquisition of developmental feeding landmarks [19]. A study in infants with GERD pointed out that a number of participants developed food refusal, which resulted in faltering growth necessitating supplementary tube feeding [20]. In an observational study of feeding disorders in infants with regular regurgitations, it was ascertained that these infants were more likely to develop feeding disorders than were control subjects [21]. Another comparative study of 20 infants with GERD reported that their dietary intake was lower, not only than that of control

Table 1 Summary of the presented studies

Study	Aim & design	Population	Key findings/comments
1 Dellert <i>et al</i> (1993) [20] Feeding resistance and gastroesophageal reflux in infancy	To identify the percentage of children with GERD who exhibited severe feeding resistance. Retrospective chart review	600 infants with GERD, age <24 months	4% of the children presented severe resistance to oral feeding resulting in supplementary tube feeding
2 Israel <i>et al</i> (1996) [26] Delayed gastric emptying as a cause of failure to thrive in children	To correlate delayed gastric emptying to poor feeding and failure to thrive. Case report	4 children aged 2 months to 3 years with failure to thrive, food refusal, and vomiting.	The only abnormal finding in these 4 children was markedly delayed gastric emptying
3 Douglas <i>et al</i> (1996) [15] Interview data on severe behavioral eating difficulties in young children	To identify any predictors of severe behavioral feeding problems. Case series	201 children with feeding problems, age 4 to 100 months	70% of the children with severe feeding problems had vomited regularly or frequently. 41% of them had a diagnosis of GERD
4 Nelson <i>et al</i> (1998) [21] One-year follow up of symptoms of gastroesophageal reflux during infancy	To determine whether infants with regular regurgitations develop feeding or mealtime problems. Case-control study	63 infants with regular regurgitations and 92 matched controls, age 6 to 12 months.	Infants with regular regurgitation at 6 to 12 months of age were more likely (19%) than control subjects (9%) to develop feeding problems within the following year
5 Mathisen <i>et al</i> (1999) [22] Feeding problems in infants with gastro-esophageal reflux disease: a controlled study	To study feeding and swallowing problems in infants with GERD and to investigate the impact of these problems on their caregivers. Case control study	20 infants with GERD aged 5-7 months and 20 matched healthy infants	Significantly more feeding problems occurred in infants with GERD. The majority of infants with GERD failed to develop age-appropriate feeding skills
6 Field <i>et al</i> (2003) [18] Correlates of specific childhood feeding problems	To examine the prevalence of possible predisposing factors for feeding problems. Retrospective chart review	349 children with feeding problems, age 1 month to 12 years	GERD was the most prevalent condition among all children (51%) and was the factor most often associated with food refusal
7 Zangen <i>et al</i> (2003) [27] Gastrointestinal motility and sensory abnormalities may contribute to food refusal in medically fragile toddlers	To investigate motility and gastric sensory abnormalities and to describe treatment in chronically ill children with food refusal. Case series	14 tube-dependent children, age 1.5 to 6 years, with food refusal and vomiting	All the patients had gastrointestinal motility and/or sensory abnormalities, including decreased gastric volume capacity and diffuse esophageal spasm
8 Pentiuik <i>et al</i> (2007) [29] Eosinophilic esophagitis in infants and toddlers	To evaluate the presentation of eosinophilic esophagitis in infants and toddlers referred to a feeding. Clinic and responses to treatment. Case series	15 children with eosinophilic esophagitis and feeding refusal (mean age 19.9±9.7 months)	13 of the 15 children showed clinical improvement in oral intake and weight gain after documented endoscopic improvement
9 Drent <i>et al</i> (2007) [23] Feeding disorders in children with gastro-esophageal reflux disease	To verify the occurrence of feeding disorders in patients with GERD. Cross-sectional study	25 children with GERD (mean age 45.68±34.22 months) and 40 control children (mean age 60.65±36.07 months)	Children with GERD presented a significantly higher prevalence of behavioral and oral motor-sensory feeding problems compared to healthy children. 92% of children with GERD had feeding disorders
10 Fortunato <i>et al</i> (2008) [30] Protein-energy malnutrition and feeding refusal secondary to food allergies	To demonstrate the importance of thorough investigation in children with feeding problems. Case report	A 21-month-old and a 34-month-old boy with protein-energy malnutrition, food allergies, GERD and eosinophilic esophagitis	Both children exhibited food refusal behavior that was probably attributable in part to food allergies

(Contd...)

Table 1 (Continued)

Study	Aim & design	Population	Key findings/comments
11 Greer <i>et al</i> (2008) [16] Caregiver stress and outcomes of children with pediatric feeding disorders treated in an intensive interdisciplinary program	To investigate the impact of an interdisciplinary feeding program in children with feeding disorders. Quasi-experiment	121 children with feeding problems, age 10 months to 13.5 years	83% of the tube-dependent children presented oropharyngeal and gastrointestinal abnormalities
12 Haas <i>et al</i> (2009) [31] Clinical presentation of feeding dysfunction in children with eosinophilic gastrointestinal disease	To demonstrate the role of the feeding specialist in the management of children with eosinophilic gastrointestinal disease. Case report	An 18-month-old boy, a 4-year-old girl and a 9-year-old boy with GERD, food allergy and eosinophilic esophagitis	All 3 children benefited from ongoing feeding therapy. Authors pointed out that eosinophilic gastrointestinal disease can disrupt development of oral feeding
13 Williams <i>et al</i> (2010) [17] Food refusal in children: a review of the literature	To discuss the definition, etiology, and interventions pertaining to food refusal. Review of the literature	38 intervention studies in children (n=218) with feeding problems	55% of the children (n=116) had gastrointestinal disorders (mainly GERD)
14 Haas (2010) [28] Feeding disorders in food allergic children	To discuss the literature published from 1980 to 2010 regarding feeding disorders in food allergic children. Review of the literature	A case series of 15 children and 2 case report studies of 5 children with eosinophilic esophagitis and food allergy	Author concluded that, despite the lack of available research, clinical observations revealed that food allergic children can present with severe feeding disorders
15 Mukkada <i>et al</i> (2010) [38] Feeding dysfunction in children with eosinophilic gastrointestinal diseases	To further characterize feeding problems in children with eosinophilic gastrointestinal disease. Retrospective study	200 children with typical growth and eosinophilic digestive disorders, age 14 to 113 months	Feeding difficulties were prevalent in children with eosinophilic gastrointestinal disease
16 Somers (2011) [33] Peanut Allergy: Case of an 11-year-old boy with a selective diet	To highlight the possibility of serious implications of a potentially life-threatening food allergy for eating behavior. Case report	11-year 8-month-old male with peanut allergy, extremely limited dietary intake and poor weight gain.	Authors pointed out that the possibility of extreme self-restriction needs to be considered when growth disturbances are identified in an individual with food allergy
17 Wu <i>et al</i> (2012) [35] Behavioral feeding problems and parenting stress in eosinophilic gastrointestinal disorders in children	To compare behavioral feeding problems and parenting stress among children with eosinophilic gastrointestinal disorders and healthy children. Case control study	92 children with eosinophilic gastrointestinal disorders (mean age 7.6±4.2 years) and 89 matched healthy controls (mean age 7.8±4.2 years)	Children with eosinophilic gastrointestinal disorders had significantly higher levels of behavioral feeding problems than healthy controls.
18 Mehta <i>et al</i> (2013) [32] Growth and nutritional concerns in children with food allergy	To describe the potential effect of avoidance diets for food allergy on nutrition and growth in children. Review of the literature	Three studies were cited, including a case control study of 92 children with eosinophilic digestive diseases	Authors concluded that children with food allergies may experience problems such as food refusal, which can lead to inadequate nutrient intake
19 Meyer <i>et al</i> (2014) [36] Feeding difficulties in children with food protein-induced gastrointestinal allergies	To investigate the occurrence of feeding difficulties in children with FPIGA. Retrospective study	437 children with FPIGA aged 1 month to 13 years	30% of children with FPIGA had feeding difficulties reported in their medical records increased to 40% as reported by parents
20 Mehta <i>et al</i> (2018) [39] Nutritional state and feeding behaviors of children with eosinophilic esophagitis and gastroesophageal reflux disease	To compare growth, nutrition and feeding behaviors in children with GERD and children with eosinophilic esophagitis. Case control study	Children with GERD (n=38) and children with eosinophilic esophagitis (n=53) aged 1 to 7 years	BPFAS problem and frequency scores were similar in GERD and eosinophilic esophagitis subjects, but were higher than those of a historical cohort of healthy controls

GERD, gastroesophageal reflux disease; FPIGA, food protein-induced gastrointestinal allergies; BPFAS, Behavioral Pediatrics Feeding Assessment Scale

subjects, but also than the recommended dietary intake. Furthermore, the majority of infants with GERD had oral motor disorders, developed higher levels of food refusal, a greater number of choking incidents and interrupted meals. Delay in developmental stages, such as the ability to hold a spoon, putting objects into the mouth and feeding autonomy, was noticed as well. Moreover, their mothers reported negative feelings regarding the feeding process and found it necessary to be present during feeding. Videofluoroscopy findings identified mainly oral phase dysphagia, as well as silent aspiration and delayed esophageal transit [22]. Another observational study pointed out that children with GERD (N=25) were more likely to show behavioral feeding disorders and oral motor delays compared with the control group (N=40). Specifically, 92% of children with GERD had feeding disorders, 44% of which involved behavioral issues and 81% oral motor problems. It is noteworthy that a high percentage of the control group (47%) also had feeding problems: 40% behavioral and 10% oral motor deficits [23]. A possible explanation for this result might be the fact that the specific study aimed to identify a broad range of feeding problems, from mild to severe, and not necessarily feeding disorders of clinical significance.

Feeding problems in children with intestinal motility disorders

Intestinal motility disorders, such as decreased gastric motility and delayed gastric emptying, may not be clinically obvious but may lead to a decrease in appetite, early satiety and food refusal, according to some researchers [18,24-27]. Israel and Mahdi reported a case series of 4 children with noticeably delayed gastric emptying who presented with failure to thrive, food refusal and vomiting. All 4 children underwent a gastric drainage procedure, which resulted in a dramatic change in food intake and a decrease in vomiting [26]. Field *et al* also reported 15 children with delayed gastric emptying who presented with feeding problems, including food refusal, selectivity and oral motor problems [18]. All of them also had GERD, which prevented the researchers from determining the impact of the delayed gastric emptying alone on the development of the feeding problems. The assumption of the authors was that the delayed gastric emptying might have exacerbated GERD and inhibited the appetite, or might have been the result of malnutrition in some of the children. Digestive tract motility disorders, including delayed gastric emptying, dysrhythmia of the antrum and diffuse esophageal spasm, were reported in 14 catheter-dependent children with food refusal who had episodes of vomiting and eructation even after fundoplication surgery [27].

Feeding problems in children with food allergies

According to the limited, but continually growing literature, children with food allergies may exhibit dysfunctional behavior, such as restricted diet, selectivity, feeding refusal,

food neophobia and generally anxiety over feeding, which can lead to reduced dietary intake, affect growth and may persist after the withdrawal of allergenic food [18,28-34,36]. The first report on the issue came from a chart review study that found food allergy to be a cause of feeding difficulty. Specifically, food allergy was reported in 21% of children with feeding disorders and in 15% of children with feeding refusal. However, the study stated that children had food allergies without further discussing the methodology of diagnosis [18]. According to a review, only 3 published studies were found on this issue from 1980-2010 [28]. The first study involved 15 children with eosinophilic esophagitis, 7 of whom with food allergy, who exhibited symptoms such as feeding refusal, low weight gain, oral defense, and vomiting episodes [29]. The other 2 were case studies of 5 children with significant feeding disorders and undernourishment. All of them were diagnosed with multiple food allergies, GERD, and eosinophilic esophagitis [30-31]. Another review cited 3 studies suggesting that maladaptive feeding behaviors in children with food allergy might affect growth [32]. One was a case report of a patient with peanut allergy [33]. The second study addressed quality of life and anxiety in patients and families with peanut allergy [34], whereas the third study discussed feeding difficulties in children with eosinophilic digestive diseases, which are separate entities [35]. A retrospective study investigated the occurrence of feeding difficulties in 437 children with food protein-induced gastrointestinal allergies (FPIGA). The most common diagnoses included non-immunoglobulin E (IgE)-mediated gastrointestinal food allergies and food protein-induced enterocolitis. The study indicated that 30% of children with FPIGA had feeding difficulties reported in their medical records, increasing to 40% reported by parents. The clinical manifestations of vomiting, constipation, rectal bleeding, and weight loss, the presence of extraintestinal manifestations and the number of foods eliminated from the diet were significantly associated with the presence of feeding difficulties [36].

Feeding problems in children with eosinophilic esophagitis

More recently, studies with strong research design provided high quality evidence to support the association between eosinophilic esophagitis and feeding problems. One case-control study investigated feeding disorders and parental stress in 92 children with eosinophilic digestive disorders using the Behavioral Pediatrics Feeding Assessment Scale (BPFAS) [35]. This scale is one of the most widely used and validated methods for detecting feeding problems [4,37]. According to the findings, children with eosinophilic disorders had significantly higher levels of behavioral feeding disorders compared to the control group. The presence of feeding disorders was more common in younger children and was positively associated with elevated levels of parental stress. A retrospective study in 200 children with typical growth and eosinophilic digestive disorders reported that 16.5% of children had severe feeding disorders. More specifically, about 94% exhibited dysfunctional behaviors such as food refusal, food selectivity and reduced

dietary intake; 85% had a tendency to vomiting or vomiting episodes; while 21% were diagnosed with failure to thrive. Of these children, 88% had food allergy and 52% other allergic diseases [38].

Another recent prospective study compared growth, nutrition and feeding behaviors in 91 children aged 1-7 with GERD and eosinophilic esophagitis using the BPFAS. Children with GERD and eosinophilic esophagitis had higher feeding behavior scores than healthy children and nearly one-third of the subjects had abnormal scores. Nevertheless, the GERD and eosinophilic esophagitis groups had both growth parameters within normal range and appropriate nutritional intake. BPFAS scores were not correlated with body mass index z-scores, age of presentation, or duration of the disease in either the GERD or the eosinophilic esophagitis group. However, a relatively strong correlation was found between weight-for-length z-score and the Parent Feelings/Strategies Frequency Score. Another interesting finding was that those on food allergen restriction diets reported significantly fewer problematic feeding behaviors than those on regular diets, suggesting that the type of eosinophilic esophagitis treatment had a significant effect on feeding behaviors. The problematic behaviors most frequently reported in both groups included taking longer than 20 min to finish a meal, preferring to drink rather than eat, and trying to negotiate what will be eaten. The child behaviors thought to be most problematic to parents included not enjoying eating, taking longer than 20 min to eat, and having a poor appetite. Most frequent problematic Parent Feelings/Strategies observed were getting frustrated and anxious during mealtimes, coaxing their child to eat, and not feeling confident that their child was getting enough to eat. The parental feelings that were most problematic to parents were getting frustrated or anxious while feeding their child, not feeling confident that their child was getting enough to eat, and feeling that their child's eating patterns hurt his/her health [39].

Concluding remarks

This review focuses on feeding problems in children with upper gastrointestinal diseases and as such it raises an important issue in pediatric gastroenterology of clinical importance for pediatricians, speech and language therapists, nutritionists or dieticians, and all health professionals dealing with pediatric patients who have chronic gastrointestinal disorders or feeding difficulties. Several clinical studies reveal that children with gastrointestinal diseases, especially those with GERD and eosinophilic esophagitis, are more likely to present with feeding problems that have a negative impact on development, growth, and psychosocial dynamics. These studies suggest that all children with gastrointestinal diseases should be regarded as vulnerable, and highlight the importance of assessing and treating feeding problems among these children in order to prevent severe complications. This is especially important when we take into consideration that most parents of children with moderate-to-severe feeding problems do not seek professional help, probably because

they consider feeding problems as a normal part of growing up [10]. A multidisciplinary approach is required to prevent the potential impact of feeding problems, improve growth, and reinforce successful reintroduction of food into the diet. Early detection and treatment of the gastrointestinal disease is crucial for the elimination of the associated feeding problems and their consequences. However, in a subset of children the associated symptoms persist, affecting feeding. In these cases an early referral to a feeding specialist is mandatory.

The existent literature provides poor quality evidence to establish a strong connection between food allergy and feeding difficulties. Food allergies might be associated with feeding difficulties, but a cause and effect relationship cannot be established robustly because of limitations such as weaknesses in study design, small sample sizes, sample variability and poor differentiation from eosinophilic esophagitis. Moreover, the diagnosis of food allergies is inadequately presented in many instances. Although the evidence of these studies is not sufficiently important to affect any clinical decision, it should function as an incentive to conduct further studies with larger samples and more robust study design.

A limitation of our review study is that we found only a limited number of case-control studies and limited information about the causal relationship between feeding disorders and gastrointestinal diseases, since most studies only reported organic factors affecting feeding, such as environmental and behavioral aspects. Moreover, we have focused on a limited range of gastrointestinal diseases. Therefore, the extent of feeding problems over the whole spectrum of gastrointestinal diseases has not been examined.

Future epidemiological studies should be carried out to determine the prevalence and specific characteristics of feeding problems in children with certain gastrointestinal disorders, such as GERD and food allergy. Further experimental studies are needed to clarify the exact causal relationship between feeding problems and gastrointestinal diseases. In addition, therapeutic options should be tested with a view to providing effective targeted interventions. Since current knowledge regarding the long-term consequences of feeding problems in this pediatric population is poor, experimental and follow-up studies should explore the long-term impact of feeding problems on growth and development in children with gastrointestinal diseases.

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