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Videofluoroscopic evaluation of the impact of capsule size and subject's age and gender on capsule swallowing

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HIGHLIGHTS

- Swallowing is influenced by the characteristics of what is being swallowed.
- There was no difference in swallowing capsules containing 0.50 mL or 0.95 mL.
- Larger capsules need more liquid ingestion to make swallowing easier.
- Individuals older than 40 years need a greater volume of liquid to swallow capsules than younger adults.

ABSTRACT – Background – People recurrently have difficulties swallowing solid medications, which can be associated with the size of the medication and the age and gender of individuals. **Objective –** To evaluate the impact of capsule size and adults' age and gender on oral and pharyngeal capsule transit during capsule swallows. **Methods –** Videofluoroscopy was used to measure capsule oral and pharyngeal transit during swallows in 49 healthy individuals (17 men and 32 women), with a mean age of 46 years (ranging from 23 to 88 years). Smaller capsules were filled with 0.50 mL of barium sulfate, and larger capsules were filled with 0.95 mL of barium sulfate; the volume of liquid ingested with the capsules was also quantified in each ingestion. The measurements included the oral preparation time, oral transit time, swallowing reaction time, time to laryngeal vestibule closure, laryngeal vestibule closure duration, pharyngeal transit time, and upper esophageal sphincter opening duration. **Results –** The capsule size did not influence either the oral or pharyngeal transit time. Increased liquid volume was ingested with larger capsules and by people older than 40 years. The oral transit time was shorter in older adults (60–88 years), and the time to laryngeal vestibule closure was longer in women. **Conclusion –** The size of large capsules did not make a difference in oral or pharyngeal transit when compared with smaller capsules. The capsule size and the participant's age influenced the volume of liquid ingested – larger capsules and older individuals required a larger volume. The capsule oral transit was faster in individuals older than 60 years.

Keywords – Deglutition; aging; gender; swallowing; drugs ingestion; sex.

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INTRODUCTION

Difficulties with oral ingestion of solid medications affect 10% to 40% of adult individuals[1-14]. Hence, people who need to take medication this way and have such difficulty may not receive adequate treatment.

In these circumstances, the administration is facilitated by modifying, macerating, splitting, or opening drugs, and patients may not take all prescribed doses[8,15-17]. When these changes are not made under pharmaceutical and/or medical supervision, they can limit the effectiveness of the medication and cause complications[6,9,18].

Swallowing is influenced by the characteristics of what is being swallowed[19-22], as well as the person's age[23-25] and gender[19,26]. These factors may influence the swallowing not only of solid and liquid foods but also capsules and tablets. The timing of capsule swallowing did not receive attention in health people.

The acceptability of orally ingested solid medications is related to the size and shape of tablets and capsules[7,11,22,27] and their taste[28]. Difficulties ingesting them (either to begin swallowing them or in the sensation that they are stuck in the pharynx) are more frequent in young adults and women[3,12,14,29,30] and are associated with a smaller mouth cavity and the higher density of taste receptors on the tongue[31].

This investigation aimed to assess the effect of capsule size, individuals' age and gender on capsule oral and pharyngeal transit. The hypothesis was that the capsule size and the subjects' age and gender affect the oral and pharyngeal transit time of the capsule, leading to longer transit time with large capsules, in older individuals and in women. It is possible that the volume of liquid ingested with each capsule is different.

METHODS

Ethics approval

This investigation was approved by the Research Ethics Committee of the University Hospital of the Ribeirão Preto Medical School at the University of São Paulo, IRB number HCRP 3735/2017. All volunteers signed an informed consent form, and their identities were kept confidential.

Participants

The study comprised 49 individuals (17 men and 32 women), aged 23 to 88 years, with a mean and standard deviation of 46 (18) years, with no complaints of swallowing changes. They were recruited by convenience sampling recruited among individuals who accompanied patients to the university hospital. The researchers contacted these potential volunteers and explained the objectives and methods of the investigations.

They were divided according to their age into the Younger Group (YG), with 20 individuals aged 23 to 39 years (mean of 28 years); the Middle-Aged Group (MG), with 15 individuals aged 40 to 59 years (mean of 49 years); and the Older Group (OG), with 14 individuals aged 60 to 88 years (mean of 67 years).

Inclusion/exclusion criteria

The volunteers did not self-report neurological, digestive, or head and neck diseases, nor had they been submitted to any thoracic or abdominal surgery.

Their everyday diet was exclusively oral, without food restrictions; they had no complaints or signs of difficulties swallowing liquid or solid foods or water, with the Eating Assessment Tool (EAT-10) scoring <3[32-34]. Some of them had complaints of discomfort when swallowing solid drugs.

The exclusion criteria were as follows: individuals with complaints and signs of dysphagia when swallowing foods or water, with EAT-10 scoring ≥ 3, with self-reported neuromuscular diseases and/or symptoms, head and neck, esophagus, or stomach cancer or surgery, or any disease that might interfere with swallowing[35], and who were taking antipsychotics[36].

Data collection

A videofluoroscopic swallowing study (VFSS) was performed with Arcomax angiography equipment (Philips, model BV 300, Veenpluis, the Netherlands), recording images at 30 frames per second. The participants were seated at an approximately 90º degree angle, maintaining their necks in the habitual posture, feet flat on the floor. Lateral images were taken from the oral cavity, pharynx, and proximal esophagus.

The participants were randomly given a sequence of two larger and two smaller hard capsules – two larger ones (#00 – length: 25 mm; diameter: 8 mm; volume: 0.95 mL) and two smaller ones (#01 – length: 20 mm; diameter: 7 mm; volume: 0.50 mL), filled at the moment of the examination with barium sulfate (Bariogel® 100%, Laboratory Cristalia, Itapira, SP, Brazil). They were also given four plastic cups with 100 mL of liquid (5 mL of 100% barium sulfate diluted in 95 mL of water), whose consistency was level 0 (thin) in the International Dysphagia Diet Standardisation Initiative (IDDSI) Framework, version 2.0[37].

Individuals were instructed as follows: "Look forward, put the capsule in your mouth, and drink the amount of liquid you normally ingest when taking medication". They were not instructed to swallow the capsules (non-cued swallows). The amount of liquid (in mL) they ingested when swallowing the capsule was verified by measuring the volume of liquid remaining in the plastic cup with an mL-graduated cylinder. Then, individuals were asked to check on a numerical scale ranging from 0 to 10 their degree of difficulty swallowing, in which 0 meant easy and 10 meant very difficult.

Videofluoroscopy analysis

The videofluoroscopic analysis was based on dynamic images of the oral and pharyngeal phases of swallowing. The qualitative analysis observed whether they moved their head; whether there was any liquid residue in the oral cavity; the number of swallows to ingest the capsule and all the liquid; whether they needed multiple (more than three) swallows; and whether there was premature liquid spill to the vallecula, liquid residue in the vallecula and pyriform sinuses, and liquid tracheal penetration and aspiration.

The following time measurements were taken, in milliseconds. Some of them had similar timing events, as previously described, but were related to capsule and liquid transit[38]:

- Oral preparation time (OPT): from bolus (capsule and liquid) retention with lip closure until the tip of the tongue was positioned behind the incisors, beginning the oral propulsive phase.
- Oral transit time (OTT): from the beginning of the capsule posterior movement (oral propulsive phase) until the capsule passed the mandible ramus.
- Swallowing reaction time (SRT): from the capsule's arrival at the mandible ramus to the first frame showing the hyoid elevation.
- Time to laryngeal vestibule closure (TLVC): from the hyoid elevation to the laryngeal vestibule closure.
- Laryngeal vestibule closure duration (LVCD): from the laryngeal vestibule closure to its opening.
- Pharyngeal transit time (PTT): from the capsule's arrival at the mandible ramus to its total passage through the upper esophageal sphincter (UES).
- UES opening (UESO): from the UES opening (the first frame the liquid bolus was inside the sphincter) to its closure (the first frame without bolus inside the sphincter, after the liquid and capsule transit).

The following capsule locations at the beginning of swallowing were considered: tongue dorsum, tongue base, vallecula, and UES. The videofluoroscopic examinations were analyzed blinded to capsule size, but not in duplicate.

Statistical analysis

The statistical analysis of the qualitative variables was performed with a Poisson generalized linear regression model with robust variance[39]. Comparisons involving continuous quantitative variables were made with the linear mixed-effects regression model (random and fixed effects). Linear mixed-effects models analyze data whose responses are grouped (more than one measure per individual) and the independence assumption between observations in the same group is not adequate[40]. The assumption in these models is that its residues have a normal distribution with a mean of 0 and constant variance. Response variable transformations were used in the situations in which this assumption was not observed. The orthogonal contrast post-test was used in the comparisons. All analyses were controlled for possible confounding factors, such as age and gender.

Continuous data were expressed as mean and standard deviation (SD) and categorical data as absolute or relative frequency. All analyses were performed with SAS 9.4 software. In all comparisons, the significance level was set at $P \leq 0.05$.

RESULTS

Thirty-one patients (63%) ingested one to six tablets, pills, or capsules a day – a mean of 1.5 in the Younger Group and Middle-Aged Group and 2.4 in the Older Group. Fourteen patients (28.6%) reported difficulties ingesting solid medications.

There was no difference in the qualitative variables between the ingestion of smaller and larger capsules. A greater volume of liquid (FIGURE 1) was ingested with larger capsules (P=0.03), by volunteers older than 40 years (P=0.01), with no difference between men and women (P=0.64).

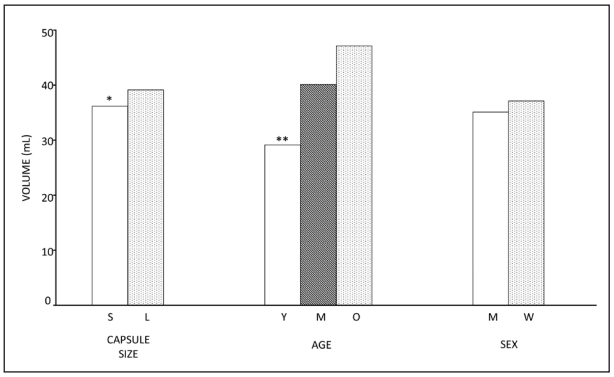

FIGURE 1. Volume of liquid ingested (mL) with smaller (S) and larger (L) capsules; in younger (Y), middle-aged (M), and older adults (O); and in men (M) and women (W). *P=0.03 vs larger; **P=0.01 vs middle-aged and older adults.

The mean number of swallows to ingest the capsules was not influenced by their size or the subject's age (smaller: Younger Group – 1.0±0.2; Middle-Aged Group – 1.1±0.3; Older Group – 1.0±0.0); larger: Younger Group – 1.1±0.4; Middle-Aged Group – 1.3±0.7; Older Group – 1.0±0.0; P>0.05).

The capsule swallowing time was not different between smaller and larger capsules (TABLE 1). The swallowing difficulty score for smaller capsules was 0.74 (1.33), ranging from 0 to 6; for larger capsules, it was 1.18 (1.84), ranging from 0 to 8 (P<0.01). Individuals who reported difficulties ingesting solid medications before the examination also had the highest difficulty scores during the videofluoroscopic examination.

The assessment verified that age did not influence the qualitative variables – except for head extension, present in 20% of swallows in the Younger Group, 13% in the Middle-Aged Group, and 0% in the Older Group (P<0.05). OPT for smaller capsules was longer in the Middle-Aged Group than in the Younger Group and Older Group (TABLE 2, P<0.05), and OTT for both capsules was shorter in the Older Group than in the Younger Group and Middle-Aged Group (TABLES 2 and 3, P<0.05).

TABLE 1. Duration, in milliseconds, of swallowing events with smaller and larger capsules in healthy subjects (n=49). Mean (SD).

	Smaller	Larger	*P*-value
OPT	2507 (985)	2503 (883)	0.48
OTT	258 (379)	244 (280)	0.70
SRT	-35 (168)	-33 (65)	0.83
TLVC	166 (227)	188 (247)	0.34
LVCD	1252 (1038)	1292 (1035)	0.27
PTT	1202 (1013)	1263 (990)	0.25
UESO	1157 (1034)	1228 (1025)	0.25

OPT: Oral preparation time; OTT: oral transit time; SRT: swallowing reaction time; TLVC: time to laryngeal vestibule closure; LVCD: laryngeal vestibule closure duration; PTT: pharyngeal transit time; UESO: upper esophageal sphincter opening; SD: standard deviation

TABLE 2. Duration, in milliseconds, of swallowing events with smaller capsules in healthy subjects divided into three age groups: younger adults (23 to 39 years, n=20), middle-aged adults (40 to 59 years, n=15), and older adults (60 to 88 years, n=14). Mean (SD).

	Younger	Middle-aged	Older
OPT	2297 (906)	3019 (1184)*	2260 (611)
OTT	268 (313)	357 (561)	139 (105)**
SRT	-17 (55)	-43 (290)	-51 (75)
TLVC	118 (210)	216 (274)	179 (186)
LVCD	898 (669)	1477 (1156)	1516 (1214)
PTT	918 (627)	1384 (1059)	1413 (1308)
UESO	866 (643)	1366 (1107)	1349 (1310)

*P<0.05 vs younger and older adults; **P<0.05 vs younger and middle-aged adults. OPT: oral preparation time; OTT: oral transit time; SRT: swallowing reaction time; TLVC: time to laryngeal vestibule closure; LVCD: laryngeal vestibule closure duration: PTT: pharyngeal transit time; UESO: upper esophageal sphincter opening; SD: standard deviation.

TABLE 3. Duration, in milliseconds, of swallowing events with larger capsules in healthy subjects divided into three age groups: younger adults (23 to 39 years, n=20), middle-aged adults (40 to 59 years, n=15), and older adults (60 to 88 years, n=14). Mean (SD).

	Younger	Middle-aged	Older
OPT	2432 (1062)	2852 (857)	2231 (406)
OTT	310 (369)	273 (231)	120 (73)*
SRT	-20 (59)	-46 (82)	-35 (52)
TLVC	123 (205)	237 (312)	228 (209)
LVCD	991 (786)	1519 (1141)	1481 (1153)
PTT	1049 (813)	1485 (1055)	1332 (1116)
UESO	1000 (813)	1491 (1148)	1272 (1119)

*P<0.05 vs younger and middle-aged adults. OPT: oral preparation time; OTT: oral transit time; SRT: Swallowing reaction time; TLVC: Time to laryngeal vestibule closure: LVCD: laryngeal vestibule closure duration; PTT: pharyngeal transit time; UESO: upper esophageal sphincter opening; SD: standard deviation.

The predominating location of the capsules when the swallowing was triggered was the tongue dorsum in the oral phase (90% for smaller and 86% for larger capsules) and the tongue base in the pharyngeal phase (90% for smaller and 88% for larger capsules), which was not influenced by the capsule size (P<0.05). Women had longer TLVC than men (TABLE 4, P=0.03), which was the only difference between the men and women in capsules swallowing.

TABLE 4. Duration, in milliseconds, of swallowing events with capsules in healthy women (n=32) and healthy men (n=17). Mean (SD).

	Women	Men	*P*-value
OPT	2627 (850)	2276 (1040)	0.11
OTT	285 (386)	190 (183)	0.36
SRT	-32 (108)	-39 (158)	0.89
TLVC	213 (244)	109 (211)	0.03*
LVCD	1322 (1000)	1179 (1098)	0.24
PTT	1257 (968)	1187 (1064)	0.30
UESO	1639 (988)	1107 (1103)	0.30

*P<0.05 women vs men. OPT: oral preparation time; OTT: oral transit time; SRT: swallowing reaction time; TLVC: time to laryngeal vestibule closure; LVCD: laryngeal vestibule closure duration; PTT: pharyngeal transit time; UESO: upper esophageal sphincter opening; SD: standard deviation.

DISCUSSION

This investigation evaluated the hypothesis that capsule size, age, and gender influence capsule ingestion. The results of the measurements indicate that their influence was small or absent.

Larger capsules did not significantly change the oral and pharyngeal transit. Even though volunteers perceived the different sizes in the oral cavity and reported greater difficulty swallowing the larger ones, once the swallowing process had started, the capsule passage time was similar. A difference in swallowing was expected between the two sizes, as the larger capsule provides different stimuli. However, this hypothesis was not confirmed.

Volunteers aged 40 to 59 years held capsules in their mouths for longer before swallowing them (i.e., oral preparation for swallowing). On the other hand, there was no difference between the group older than 60 years and the younger people, which indicates that aging is likely not responsible for the difference. It was speculated that older adults are more adapted to ingesting capsules than younger and middle-aged ones because they take medications more often. The perception of taste and the characteristics of the bolus in the oral cavity are complex issues that result from the interaction of various factors (including aging)[41]. Moreover, the integrity of oral sensitivity is essential to safe swallowing[42,43].

Head extension during swallows decreases OTT[44] and facilitates the opening of the airway. However, this head movement was not seen in the older group. The partial loss of sensitivity in the aging process[45,46] may be the explanation for the faster OTT observed in older volunteers. The sensitivity is involved in controlling the swallowing phases[42,43].

The women's longer TLVC agrees with the average slower passage of bolus through the pharynx in women than in men[26], as well as other swallowing differences between men and women[47,48]. Women were expected to have greater difficulties swallowing capsules, as there are indications that they have a smaller capacity to retain volume in the oral cavity than men[49] – which may be one of the reasons why they report difficulties[31]. Although men may have the capacity to retain a greater volume in their oral cavity, the difference between theirs and the women's oral cavity may not be enough to explain greater difficulties with medications.

The location of the capsule before swallowing was predominantly in the tongue dorsum when triggering the oral phase and in the tongue base when triggering the pharyngeal phase, for both capsule sizes. The capsule size did not have the same effect on swallowing as the increase in liquid bolus volume[50].

The liquid volume to swallow the capsule was lower with small capsules and in younger volunteers. The difference related to capsule size was small, whereas the age effect on liquid volume was more intense, suggesting that the increase in liquid volume ingested was related to difficulty in swallowing, the increase of capsule size, and older participants. The larger volume of liquid ingested may be involved with the faster oral transit seen in older participants and is related to the whole capsule ingestion process, which may cause volume ingestion even after the capsule is already swallowed.

The increase in swallowed bolus volume, which is the case of liquid ingested with the larger capsules,

changes the swallowing dynamics. It causes an early onset of anterior tongue base movement, superior palatal movement, anterior laryngeal movement, and early upper esophageal sphincter opening[50]. The larger bolus volume also lengthens the upper esophageal sphincter opening and enlarges the sphincter diameter[51]. Swallowed bolus volume is positively correlated with the magnitude of the superior and anterior hyoid movement[52]. The increase in bolus volume ingested does not change the oral and pharyngeal transit of the capsules, although it may facilitate capsule ingestion.

The capsules are larger than those (15 mm) described as a possible cause of choking[53]. This possibility must be considered in the case of older individuals and patients with dysphagia.

This investigation has limitations. It would have been useful to assess even older adults, with a predominance of people above 70 years old. Individuals reporting difficulties swallowing solid medications may make a difference when present in the various study groups. The comparison between capsules with a greater difference in size may lead to different conclusions. The measurement was not performed in duplicate, which is a limitation.

CONCLUSION

The capsule sizes approached in the study did not cause different oral or pharyngeal transit durations. Compared to smaller ones, larger capsules needed more liquid ingestion to make swallowing easier. Individuals older than 40 years needed a greater volume of liquid to swallow capsules than younger adults, with faster oral transit in individuals older than 60 years.

Authors' contribution

The authors Gutierres LFS, Montaldi MR, Nascimento WV and Dantas RO participated sufficiently in the work to take public responsibility for appropriate portions of the content. They participated in the design of the study, data acquisition and interpretation, initial manuscript writing, and approval of the final version for submission.

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Gutierres LFS, Montaldi MR, Nascimento WV, Dantas RO. Avaliação videofluoroscópica do impacto do tamanho da cápsula, idade e gênero dos indivíduos na ingestão de cápsulas. Arq gastroenterol. 2024;61:e23092.

RESUMO – Contexto – Algumas pessoas apresentam recorrentemente dificuldades para engolir medicamentos sólidos, o que pode estar associado ao tamanho do medicamento, à idade e ao gênero dos indivíduos. **Objetivo** – Avaliar, em adultos, o impacto do tamanho da cápsula, da idade e do gênero no trânsito oral e faríngeo de cápsulas. **Métodos –** Videofluoroscopia foi utilizada para medir o trânsito oral e faríngeo de cápsulas em 49 indivíduos saudáveis (17 homens e 32 mulheres), com idade média de 46 anos (limites de 23 e 88 anos). Cápsulas menores foram preenchidas com 0,50 mL e cápsulas maiores foram preenchidas com 0,95 mL de sulfato de bário; o volume de líquido ingerido com as cápsulas foi quantificado em cada ingestão. Foram medidos o tempo de preparo oral, tempo de trânsito oral, tempo de reação da deglutição, tempo para fechamento do vestíbulo laríngeo, tempo de fechamento do vestíbulo laríngeo, tempo de trânsito faríngeo e tempo de abertura do esfíncter superior do esôfago. **Resultados** – O tamanho da cápsula não influenciou o tempo de trânsito oral ou faríngeo. Mais líquido foi ingerido com cápsulas maiores e por pessoas com mais de 40 anos. O tempo de trânsito oral foi menor em idosos (60–88 anos) e o tempo de fechamento do vestíbulo laríngeo foi maior em mulheres. **Conclusão –** O tamanho da cápsula não influenciou o trânsito oral e faríngeo, porém houve maior volume de líquido ingerido com a cápsula maior e nos mais idosos. O trânsito oral da cápsula foi mais rápido em indivíduos com mais de 60 anos.

Palavras-chave – Deglutição; envelhecimento; sexo; ingestão de drogas; gênero.

REFERENCES

1. Tordoff JM, Bagge ML, Gray AR, Campbell AJ, Norris PT. Medicine-taking practices in community-dwelling people aged = 75 years in New Zealand. Age Ageing. 2010;39:574-80.
2. Mehuys E, Dupond L, Petrovic M, Christiaens T, Van Bortel L, Adriaens E, et al. Medication management among home-dwelling older patients with chronic diseases: possible roles for community pharmacists. J Nutrition Health Aging. 2012;16:721-6.
3. Schiele JT, Quinzler R, Klimm H, Pruszydlo MG, Haefeli WE. Difficulties swallowing solid oral dosage forms in a general practice population: prevalence, causes, and relationship to dosage forms**.** Eur J Clin Pharmacol. 2013;69:937-48.
4. Marquis J, Schneider M, Payot V, Cordonier A, Bugnon O, Hersberger KE, et al. Swallowing difficulties with oral drugs among polypharmacy patients attending community pharmacies. Int J Clin Pharm. 2013; 35:1130-6.
5. Lau ETL, Steadman KJ, Mak MK, Cichero JAY, Nissen LM. Prevalence of swallowing difficulties and medication modification in customers of community pharmacists. J Pharm Pract Res. 2015;45:18-23.
6. Fields J, Go JT, Schulze KS. Pill properties that cause dysphagia and treatment failure. Curr Ther Res Clin Exp. 2015;77:79-82.
7. Liu F, Ghaffur A, Bains J, Hamdy S. Acceptability of oral solid medicines in older adults with and without dysphagia: a nested pilot validation questionnaire based observational study. Int J Pharm. 2016;512:374-81.
8. Tahaineh L, Wazaify M. Difficulties in swallowing oral medications in Jordan. Int J Clin Pharm. 2017;39:373-9.
9. Oad MA, Miles A, Lee A, Lambie A. Medicine administration in people with Parkinson's disease in New Zealand: An interprofessional, stakeholder-driven online survey. Dysphagia. 2019;34:119-28.
10. Punzalan C, Budnitz DS, Chirtel SJ, Geller AL, Jones OE, Mozersky RP, et al. Swallowing problems and dietary supplements: Data from U.S. Food and Drug Administration. Adverse Event Reports, 2006–2015. Ann Intern Med. 2019;171:771-3.
11. Drumond N, Stegemann S. Better medicines for older patients: considerations between patient characteristics and solid oral dosage form designs to improve swallowing experience. Pharmaceutics. 2020;13:32.
12. Souza LF, Nascimento WV, Alves LMT, Silva ACV, Cassiani RA, Alves DC, et al. Medication swallowing difficulties in people without dysphagia. Rev CEFAC. 2019;21:e0119.
13. Oliveira MPF, Novaes MRCG. Uso de medicamentos por idosos de instituições de longa permanência, Brasília-DF, Brasil. Rev Brasil Enferm (Brasília). 2012;65:737-44.
14. McCloskey AP, Penson PE, Tse Y, Abdelhafiz MA, Ahmed SN, Lim EJ. Identifying and addressing pill aversion in adults without physiological-related dysphagia: a narrative review. Br J Clin Pharmacol. 2022;88:5128-48.
15. Mercovich N, Kyle GJ, Naunton M. Safe to crush? A pilot study into solid dosage form modification in aged care. Australas J Ageing. 2014;33:180-4.
16. Ganzetti R, Logrippo S, Sestili M, Caraffa A, Cespi M, Pelliccioni G, et al. Tablet splitting in elderly patients with dementia: the case of quetiapine. Pharmaceutics. 2021;13:1523.
17. Robert V, Fabri B, Bouillot E, Papailhau C, Abbes M, Grino M, et al. A description of dry oral forms of medication administration modifications by nurses in home settings. Geriatr Nurs. 2022;43:249-53.
18. Lau ETL, Steadman KJ, Cichero JAY, Nissen LM. Dosage form modification and oral drug delivery in older people. Adv Drug Deliv Rev. 2018;135:75-84.
19. Ferris L, Doeltgen S, Cock C, Rommel N, Schar M, Carrion S, et al. Modulation of pharyngeal swallowing by bolus volume and viscosity. Am J Physiol. 2021;320:G43-53.
20. Lenell C, Brates D, Pearson Jr WG, Molfender S. Variations in healthy swallowing mechanics during various bolus conditions using computational analysis of swallowing mechanics (CASM). Dysphagia. 2020;35:272-80.
21. Steele CM, Peladeau-Pigeon M, Barbon CAE, Guidda BT, Tapson MS, Valenzano TJ, et al. Modulation of tongue pressure according to liquid flow properties in healthy swallowing. J Speech Lang Hear Res. 2019;62:22-33.
22. Hummler H, Page S, Stillhart C, Meilicke L, Grimm M, Mannaa M, et al. Influence of solid oral dosage characteristic on swallowability, visual perception, and handling in older adults. Pharmaceutics. 2023;15:1315.
23. Mancopes R, Gandhi P, Smaoui S, Steele CM. Which physiological swallowing parameters change with healthy aging? OBM Geriat. 2021;5:153.
24. Ishak AG, Cherukuri S, Diaz G, McCallum R. Dysphagia in the older age setting. OBM Geriatrics. 2021;5:174.
25. Namasivayam-MacDonald AM, Barbon CEA, Steele CM. A review of swallow timing in the elderly. Physiol Behav. 2018;184:12-26.
26. Dantas RO, Cassiani RA, Santos CM, Gonzaga GC, Alves LM, Mazin SC. Effect of gender on swallow event duration assessed by videofluoroscopy. Dysphagia. 2009;24:280-4.
27. Hansen DL, Tulinius D, Hansen EH. Adolescents' struggles with swallowing tablets: barriers, strategies and learning. Pharm World Sci. 2008;30:65-9.
28. Schiele JT, Penner H, Schneider H, Quinzer R, Reich G, Wezler N, et al. Swallowing tablets and capsules increases the risk of penetration and aspiration in patients with stroke-induced dysphagia. Dysphagia. 2015;30:571-82.
29. Lorca PM. Discussion of prevalence and management of discomfort when swallowing pills: orodispersible tablets expand treatment options in patients with depression. Ther Deliv. 2011;2:611-22.
30. Andersen O, Zweidorf OK, Hjeide T, Rodland EA. Problems when swallowing tablets. A questionnaire study from general practice. Tidsskr Nor Laegeforen. 1995;115:947-9.
31. Radhakrishnan C, Sefidani Forough A, Cichero JAY, Smyth HE, Raidhan A, Nissen LM, et al. A difficult pill to swallow: an investigation of the factors associated with medication swallowing difficulties. Patient Prefer Adherence. 2021;15:29-40.
32. Belafsky PC, Mouadeb DA, Rees CJ, Pryor JC, Postma GN, Allen J, et al. Validity and reliability of the Eating Assessment Tool (EAT-10). Ann Otol Rhinol Laryngol. 2008;117:919-24.
33. Gonçalves MIR, Remaili CB, Behlau M. Cross-cultural adaptation of the Brazilian version of the Eating Assessment Tool – EAT-10. CoDAS. 2013;25:601-4.
34. Dantas RO, Alves LMT, Silva ACV, Cassiani RA, Alves DC, Nascimento WV. Eating Assessment Tool (EAT-10 scores to detect self-reported dysphagia in Brazilians. Dysphagia. 2023;39:1609-14.
35. Clavé P, Shaker R. Dysphagia: current reality and scope of the problem. Nat Rev Gastroenterol Hepatol. 2015;12:259-70.
36. Cicala G, Barbieri MA, Spina E, de Leon J. A comprehensive review of swallowing difficulties and dysphagia associated with antipsychotics in adults. Expert Rev Clin Pharmacol. 2019;12:219-34.
37. Cichero JAY, Lam PTL, Chen J, Dantas RO, Duivestein J, Hanson B, et al. Release of updated International Dysphagia Diet Standardisation Initiative Framework (IDDSI 2.0). J Texture Stud. 2020;51:195-6.
38. Steele CM, Barrett E, Peladeau-Pigeon M. Which videofluoroscopy parameters are susceptible to influence of differences in barium product and concentration? Am J Speech Lang Pathol. 2022;31:2145-58.
39. Zou G. A modified Poisson regression approach to prospective studies with binary data. Am J Epidemiology. 2004;159:702-6.
40. Schall R. Estimation in generalized linear models with random effects. Biometrika. 1991;78:719-927.
41. Alia S, Aquilanti L, Pugnaloni S, Di Paolo A, Rappelli G, Vignini A. The influence of age and oral health on taste perception in older adults: A case-control study. Nutrients. 2021;13:4166.
42. Gould FDH, Ohlemacher J, Lammers AR, Gross A, Ballester A, Fraley L, et al. Central nervous system integration of sensorimotor signals in oral and pharyngeal structures: oropharyngeal kinematics response to recurrent laryngeal nerve lesion. J App Physiol. 2016;120:495-502.
43. Steele CM, Miller AJ. Sensory input pathways and mechanisms in swallowing: A review. Dysphagia 2010;25:323-33.
44. Sugiyama S, Iida T, Morimoto Y, Yamazaki Y, Mikuzuki L, Hayashi M. Effects of tablet size and head posture on drug swallowing: a preliminary examination using endoscopy in healthy subjects. Acta Med Okayama. 2021;75:495-503.
45. Zhang L, Shimeda A, Kusunovi T, Inoue T, Kawamoto A, Takahashi K. Effect of ageing and tooth loss on sensory function of alveolar mucosa. J Oral Rehabil. 2022;49:391-7.
46. Wang M, Septier C, Brignot H, Martin C, Canon F, Feron G. Astringency sensitivity to tannic acid: effect of ageing and saliva. Molecules. 2022;27:1617.

47. Endo H, Ohmori N, Chikai M, Miwa H, Ino S. Effects of age and gender on swallowing activity assessed by electromyography and laryngeal elevation. J Oral Rehabil. 2020;47:1358-67.
48. Watanabe S, Izuhara E, Oh-Shige H, Miyashi H, Goto M, Hasegawa S, et al. Relationship between age and sex and the numbers of ingestions and swallows for food of different textures among healthy adults. Physiol Behav. 2021;229:113225.
49. Nascimento WV, Cassiani RA, Dantas RO. Gender effect on oral volume capacity. Dysphagia. 2012;27:384-9.
50. Dantas RO, Kern MK, Massey BT, Dodds WJ, Kahrilas PJ, Brasseur JG, et al. Effect of swallowed bolus variables on oral and pharyngeal phases of swallowing. Am J Physiol 1990;258:G675-81.
51. Kahrilas PJ, Dodds WJ, Dent J, Logemann JA, Shaker R. Upper esophageal sphincter function during deglutition. Gastroenterology. 1988;95:53-62.
52. Dodds WJ, Man KM, Cook IJ, Kahrilas PJ, Stewart ET, Kern MK. Influence of bolus volume on swallow-induced hyoid movement in normal subjects. Am J Roentgenol. 1988;150:1307-9.
53. Bandini A, Ghandi P, Sutton D, Steele CM. Bolus texture testing as a clinical method for evaluation food oral processing and choking risk: a pilot study. Am J Speech Lang Pathol. 2022;31:2806-16.