

# Mortality in Cleft Lip and Palate Patients: A Systematic Review and Meta-analysis

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**Background:** Cleft lip and/or palate (CLP) represents one of the most common congenital anomalies among live births globally. Morbidity associated with CLP is well documented in the literature and stratified through measures such as disability-adjusted life years. However, a paucity of literature details mortality rates among different subgroups of patients with CLP.

**Methods:** A meta-analysis was performed using preferred reporting items for systematic reviews and meta-analysis guidelines. Included studies reported on mortality rates of patients with CLP in a liveborn cohort. Studies that reported only intraoperative mortality, included fetal mortality, or included non-CLP conditions in mortality rates were excluded. Meta-analysis was performed through subgroup analysis using random-effects models.

**Results:** Twenty-one studies were included. Mortality rates ranged from 1.22% to 19.8% between studies. Patients with isolated cleft lip had lower odds of mortality compared with CLP (odds ratio [OR] = 0.28 [0.14, 0.56],  $P = 0.005$ ) or isolated palate (OR = 0.34 [0.24, 0.48],  $P = 0.0005$ ). Increased odds of mortality were found in patients with comorbidities (OR = 19.79 [11.37, 34.43],  $P < 0.0001$ ) compared with otherwise healthy CLP patients. Across age groups, neonates (0–28 d) had the highest mortality rate (0.7%–19.8%) followed by infants (0.2%–6.6%), both with  $P$  values less than 0.05.

**Conclusions:** Mortality rates in patients with CLP are higher for those with an additional comorbidity or younger age (<1 y). Further studies stratifying data by cleft phenotype and age are required to better understand factors that contribute to CLP mortality. (*Plast Reconstr Surg Glob Open* 2025;13:e6721; doi: 10.1097/GOX.0000000000006721; Published online 1 May 2025.)

## INTRODUCTION

Orofacial clefting (OFC) is a common congenital malformation globally. One of the most common types of OFC is cleft lip and/or palate (CL/P), with incidence rates ranging from 1 in 700 to 1 in 1000 live births.<sup>1–4</sup> Infants born with congenital abnormalities such as OFC are subject to greater morbidity and mortality compared with unaffected births.<sup>5–7</sup> The morbidity of cleft conditions extends beyond the well-known physical limitations, such

as speech and nutrition. For example, children with OFC often face difficulties at school such as bullying and elevated prevalence of mental health conditions.<sup>8–10</sup> The burden of disease for OFCs has been extensively quantified and reported through the use of disability-adjusted life years at regional and global levels.<sup>2,11,12</sup> Dedicated research into cleft morbidity has led to the implementation of structured multidisciplinary teams to address patient needs.<sup>13</sup>

In contrast to morbidity, mortality rates related to OFC are less frequently reported. In the 2021 Global Burden of Disease study, OFC mortality data were only published for a single country, based on 3 sources.<sup>14</sup> Such scarcity in data, despite the collaborative effort of the study, demonstrates the significant gap in the literature pertaining to OFC mortality. A critical challenge to understanding cleft mortality is the presence of comorbidities or other associated malformations seen in syndromic cases, which occurs in approximately

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30% of patients. The most frequently reported syndromes among cleft patients include Van der Woude and Velocardiofacial syndromes, whereas heart disease, gastrointestinal pathologies, and respiratory pathologies are common isolated malformations.<sup>15,16</sup> Compared with patients with isolated clefts, comorbid patients possess a greater risk of complications and require additional specialist multidisciplinary management. These circumstances may confound our ability to quantify the mortality of OFC alone.<sup>17,18</sup> The presence of coexisting conditions likely increases mortality due to the increased burden of disease. However, studies evaluating the difference in mortality between healthy versus comorbid patients with cleft conditions are not readily available.

Furthermore, it has been well established that globally, mortality rates vary between children of different age groups.<sup>19,20</sup> Neonatal mortality is often greater than that of older children, but minimal literature exists describing OFC mortality among patients of different ages. Another factor that may impact mortality rates is the cleft phenotype. Surgical outcomes and morbidity are often worse in more complex phenotypes, yet their impact on mortality is scarcely reported.<sup>21,22</sup>

Given the paucity of data on OFC-related mortality, the aim of this study was to specifically evaluate mortality associated with CL/P. The primary objective was to determine the overall mortality rate of patients with cleft and no additional comorbidities compared with patients with clefts who had 1 or more additional congenital comorbidities. The secondary objective was to assess mortality differences between age groups in patients with CL/P.

### Takeaways

**Question:** What is the overall mortality in patients with a cleft lip or palate across different phenotypes, ages, and comorbidity status?

**Findings:** We included 21 articles in this meta-analysis. Mortality rates ranged from 1.22% to 19.8%. Patients with isolated cleft lip had lower odds of mortality compared with cleft lip and palate or isolated palate. Increased odds of mortality were found in patients with comorbidities compared with otherwise healthy patients. Neonates had the highest mortality rate of all age groups.

**Meaning:** Mortality rates in patients with cleft are higher for those with clefts of the palate, additional comorbidities, or younger age. These factors should be considered when planning management.

### METHODS

A systematic review and meta-analysis were performed of the PubMed, Cochrane, and Scopus databases from inception until April 2024 in accordance with preferred reporting items for systematic reviews and meta-analysis guidelines.<sup>23</sup> The search strategy flowchart is shown in Figure 1. Search terms included: “cleft lip,” “cleft palate,” “orofacial cleft,” “mortality,” “death rate,” and “death.” References of selected articles were also reviewed to identify any articles that may have been missed with the database search. Included studies were English-language articles that reported mortality rates for patients with OFC (if the rate was calculable based on available data, it was included), and mortality rates only included live births. The following

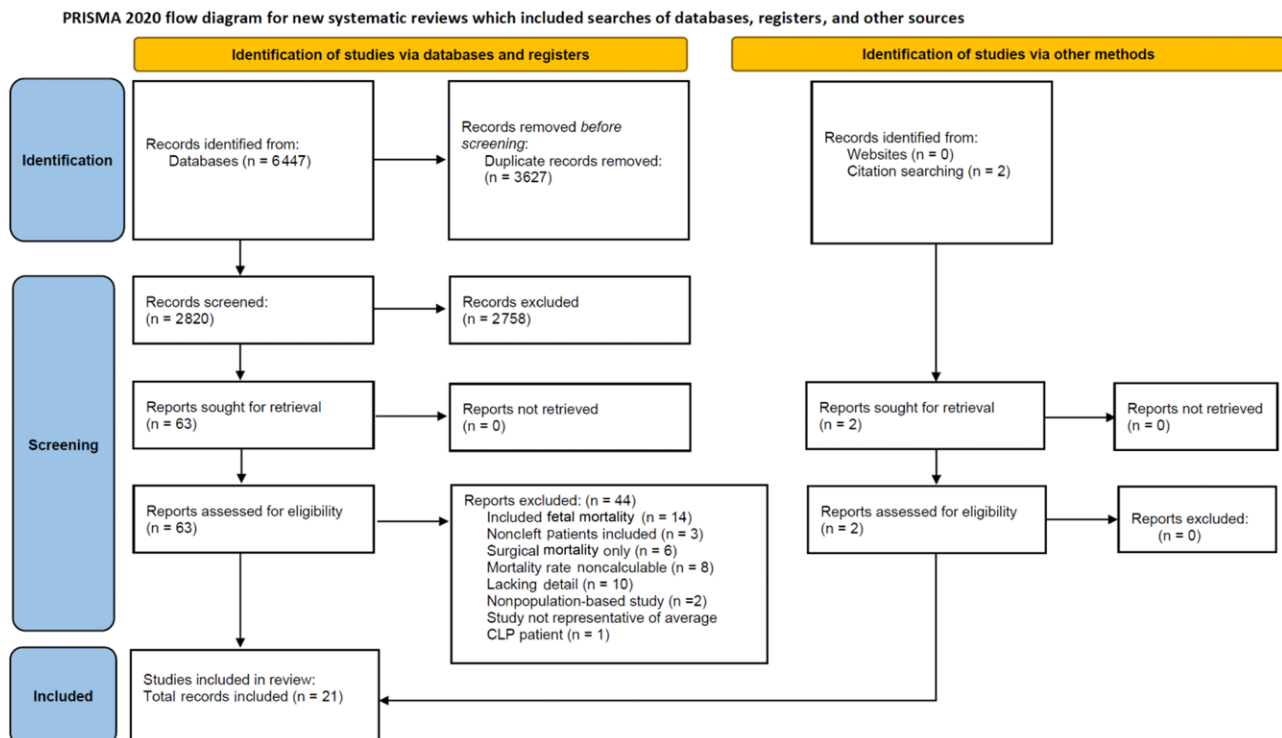


Fig. 1. PRISMA flow diagram of the search strategy. PRIMA, preferred reporting items for systematic reviews and meta-analysis.

studies were excluded: reports of intraoperative mortality as opposed to postoperative mortality, studies documenting fetal mortality, studies with inadequate data, inclusion of noncleft lip and palate conditions in reported mortality rate, review papers, and comparative studies of multiple populations with cleft lip and palate (CLP). Inadequate data were defined as studies reporting data in a manner that precluded assessment or calculation of mortality rate among a cleft patient cohort. Search results were screened by title, followed by abstract and full-text screening to assess fit with decided criteria. Quality assessment of included studies was performed using the Newcastle-Ottawa scale. Title and abstract screening was performed by 1 author (A.T.P.), and the inclusion of studies in the analysis was agreed upon by 2 authors (A.T.P. and P.N.). There were no disagreements regarding study inclusion.

General characteristics about each study were collected: first author name, year of publication, country of study, length of follow-up, and type of study. Data extracted included total patients, socioeconomic status of patients, mortality rate either reported or calculated, causes of death among each cohort, and number of patients by cleft phenotype. Phenotypes were grouped as cleft lip only (CL), CLP, and cleft palate only (CP). Patients were stratified as comorbid or noncomorbid with a comorbidity defined as any additional genetic, syndromic, or physical congenital pathology. Patients were also stratified into 4 groups according to age: 0–28 days (neonate), 28 days to 1 year (infant), 1–5 years, and 5+ years. These age groups were selected based on conventionally reported groups in population-based mortality studies. If studies reported a combined age range of 0–1 years, this age range was recorded but not used in further data analysis. If studies reported the mortality rate of a matched, unaffected infant cohort or the overall infant mortality rate of their region, these data were also recorded. Data were aggregated and organized in Microsoft Excel (Microsoft Corporation, Redmond, WA).

Meta-analysis of data began with plotting the overall mortality reported in each study on a forest plot. Wald confidence intervals were calculated, and the Agresti–Coull correction was applied to account for low event rates. We subsequently conducted subgroup meta-analyses utilizing odds ratios (ORs). Selected subgroups were (1) cleft phenotype, (2) presence or absence of comorbidity, and (3) age group. Random-effects models were fit to each subgroup comparison, and study heterogeneity was confirmed using the  $I^2$  statistic. Significance was set at  $P$  equal to 0.05 for hypothesis testing, and all confidence intervals were reported at a 95% level. Statistical analysis was performed in R Statistical Software (Version 4.3.2; R Core Team 2024).

## RESULTS

### General Characteristics

Following the application of inclusion and exclusion criteria, a total of 21 articles were included in the review.<sup>24–44</sup> Characteristics of selected articles are displayed in Supplemental Digital Content 1. (See table, Supplemental Digital Content 1, which displays the general

study characteristics, <http://links.lww.com/PRSGO/D980>.) Articles were most commonly from the United States ( $n = 8$ , 38.1%), the United Kingdom ( $n = 4$ , 19%), and Australia ( $n = 2$ , 9.5%). Each study included between 59 and 19,218 patients. The most common length of follow-up was 1 year ( $n = 10$ , 47.6%), followed by 5+ years ( $n = 5$ , 23.8%).

### Overall Mortality and Mortality by Cleft Phenotype

The overall mortality rate of CL/P patients ranged from 1.22% to 19.8% with a median of 8.94% (interquartile range [IQR] = 7.5) (Fig. 2). Nine (42.9%) studies reported a matched unaffected control cohort without any additional comorbidities. Among the control patients, the mortality rate ranged from 0.29% to 2.2% with a median of 0.8% (IQR = 1.0). Stratified by country income status, in high-income countries, mortality ranged from 1.22% to 14.6% with a median of 8.78% (IQR = 7.9); in low- and middle-income countries (LMICs), the range was 7.82% to 19.8% with a median of 10.20% (IQR = 6.0). Looking at cleft phenotype, mortality rates for patients ranged from 0.64% to 7.1% (median = 1.76%, IQR = 2.28) for CL, 0.53%–15.5% (median = 8.4%, IQR = 12.62) for CLP, and 2.45%–20.3% (median = 9.35%, IQR = 7.86) for CP (Table 1). Patients with CL had significantly lower odds of mortality compared with patients with CLP (OR = 0.28 [0.14, 0.56],  $P = 0.005$ ) and CP (OR = 0.34 [0.24, 0.48],  $P = 0.0005$ ). No significant difference was found in odds of mortality between the CLP and CP groups ( $P = 0.94$ ). Full details of the random-effects models are available in Supplemental Digital Content 2. (See table, Supplemental Digital Content 2, which displays the full details of the random-effects models comparing different cleft phenotypes, <http://links.lww.com/PRSGO/D981>.)

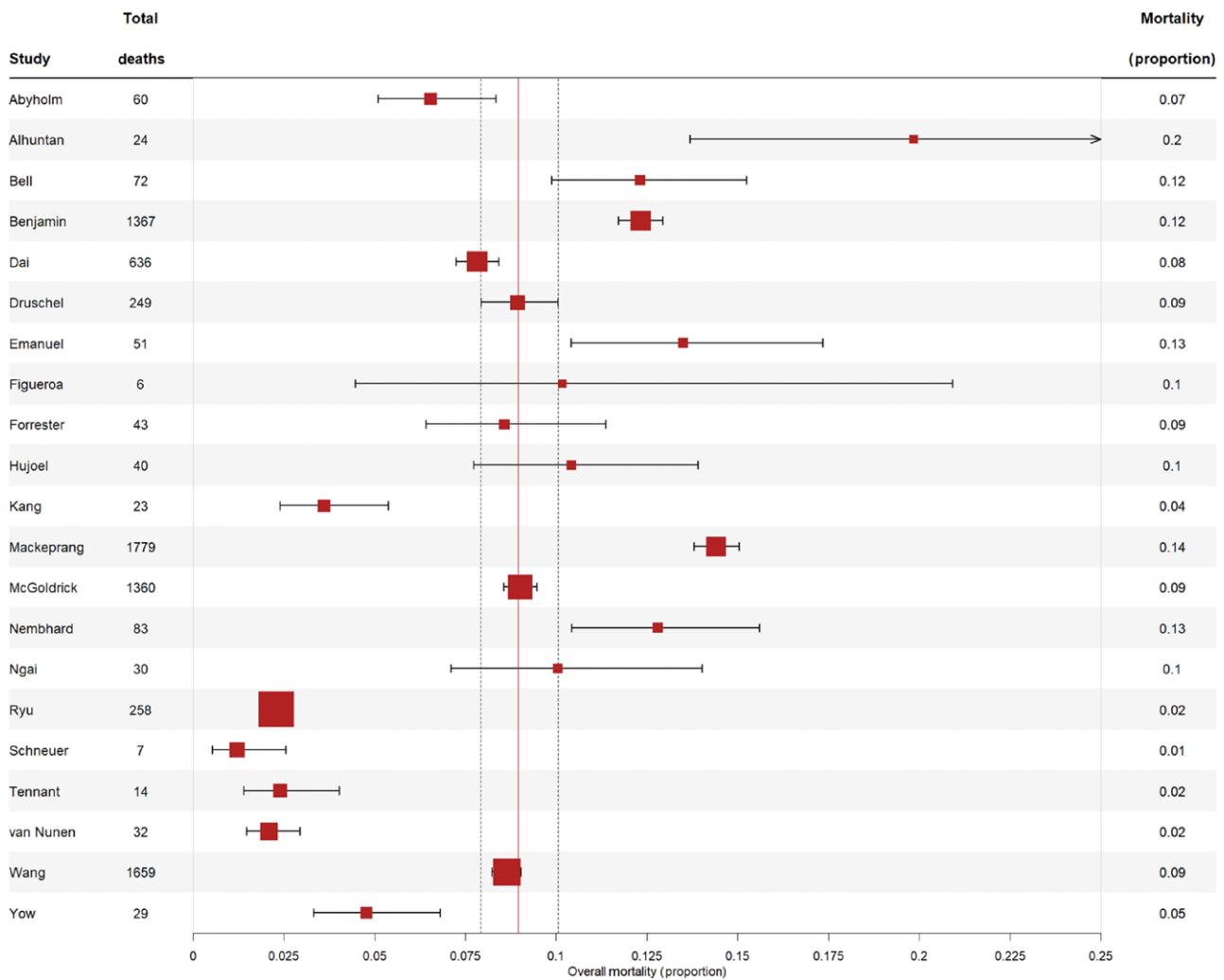
Causes of death among patients were reported by 5 (23.8%) of the articles. However, causes reported by studies were nonspecific, precluding additional analysis. Furthermore, deaths related to complications from noncleft surgical procedures were not reported in the included studies.

### Mortality by Comorbidity

The mortality rate for patients with noncomorbid cleft ranged from 0% to 5.76% (median = 1.64%, IQR = 2.27) versus 7.55% to 52.75% (median = 23.48%, IQR = 20.54) for patients with comorbid clefts (Table 2). The presence of a comorbidity significantly increased the odds of mortality (OR = 19.79 [11.37, 34.43],  $P < 0.0001$ ). On subgroup analysis of the 3 cleft phenotypes across comorbid and noncomorbid patients, increased odds of mortality in comorbid patients were found for CL (OR 9.8 [4.12, 23.3],  $P = 0.008$ ), CLP (OR 17.45 [1.74, 175.1],  $P = 0.03$ ), and CP (OR = 18.88 [9.25, 38.52]  $P < 0.0001$ ). (See table, Supplemental Digital Content 3, which displays the full details of the random-effects models comparing comorbid to noncomorbid [isolated] patients, <http://links.lww.com/PRSGO/D982>.)

### Mortality by Age Group

Mortality ranges were 0.7%–19.8% (median = 5.7%, IQR = 4.5) for neonates (0–28 d), 0.2%–6.6%



**Fig. 2.** Forest plot of overall mortality among included articles. Confidence intervals are at the 95% confidence level. The solid red line represents the median mortality proportion, and the dashed lines are the 95% confidence interval of the median value.

(median = 2.27%, IQR = 2.05) for infants (1 mo to 1 y), 0%–1.4% (median = 0.45%, IQR = 0.835) for children 1–5 years of age, and 0.18%–0.5% (median = 0.22%, IQR = 0.11) for patients older than 5 years (Table 3). Neonates had a significantly increased odds of mortality compared with all other age groups: infants (OR = 1.8 [1.02, 3.18],  $P = 0.044$ ), 1–5 years (OR = 8.17 [1.66, 40.19],  $P = 0.022$ ), and older than 5 years (OR = 25.21 [12.25, 51.86],  $P = 0.003$ ). Infants had significantly increased odds of mortality compared with children 1–5 years of age (OR = 1.77 [1.93, 11.76],  $P = 0.009$ ), and trended toward an increased odds of mortality compared with those older than 5 years (OR = 8.19 [0.99, 67.57],  $P = 0.0504$ ). Mortality odds did not differ between the 1–5 years and older than 5 years of age groups (OR = 1.56 [0.19, 12.79],  $P = 0.461$ ). There were insufficient data to further stratify and analyze age groups according to phenotype or comorbidity. (See table, Supplemental Digital Content 4, which displays the full details of the random-effects models comparing different age groups of cleft patients, <http://links.lww.com/PRSGO/D983>.)

## DISCUSSION

Although morbidity related to CLP is well reported, existing data on CLP mortality is sparse and often lacks granularity. Nevertheless, a comprehensive understanding of factors contributing to mortality in patients with OFC is imperative to both surgical planning and communication with patient families. In this systematic review and meta-analysis on CLP mortality, we found a reported mortality rate in cleft patients ranging from 1.2% to 19.8%, suggesting that CLP mortality is comparable to some of the most common congenital anomalies globally. The prevailing risk factor for mortality was the presence of additional comorbid conditions. Children born with CLP are 20 times more likely to die if they have an associated comorbidity across all cleft phenotypes. Furthermore, odds of mortality were greatest earlier in life, with an 8 times increased odds of death in neonates and 1.8 times increased odds in infants compared with patients older than 1 year.

Our study found a significant difference between mortality rates among CL, CLP, and CP. Lip-only patients had one-third the odds of mortality compared with the



**Table 1. Overall Mortality of Patients With OFC and Mortality Rate Between Different Phenotypes**

Author	Overall Mortality Rate, %	Total No. CL Patients	Mortality Rate CL, %	Total No. CLP Patients	Mortality Rate CLP, %	Total No. CP Patients	Mortality Rate CP, %	Unaffected Mortality Rate, %
Abyholm <sup>24</sup>	6.54	297	—	380	—	241	—	—
Altunhan et al <sup>25</sup>	19.80	—	—	86	—	35	—	—
Bell et al <sup>26</sup>	12.30	—	2.30	—	15.50	—	16.50	1.40
Benjamin et al <sup>27</sup>	12.31	—	—	—	—	3873	13.80	—
Dai et al <sup>28</sup>	7.82	2553	3.10	4325	10.50	1255	8.10	—
Druschel et al <sup>29</sup>	8.94	—	—	1599	8.40	1187	9.70	0.77
Emanuel et al <sup>30</sup>	13.49	89	3.40	161	15.50	128	18	2.20
Figueroa et al <sup>31</sup>	10.17	—	—	—	—	—	—	—
Forrester and Merz <sup>32</sup>	8.57	—	—	—	—	181	8.80	—
Hujoel et al <sup>33</sup>	10.32	—	—	—	—	130	15.40	0.80
Kang et al <sup>34</sup>	3.61	142	0.70	188	0.53	308	6.82	0.41
Mackeprang and Hay <sup>35</sup>	14.64	3378	7.10	5328	15.00	3646	20.30	—
Mc Goldrick et al <sup>36</sup>	9.00	—	—	—	—	—	—	—
Nembhard et al <sup>37</sup>	12.79	—	—	—	—	246	13.40	—
Ngai et al <sup>38</sup>	10.00	—	—	—	—	—	—	—
Ryu et al <sup>39</sup>	2.29	2323	0.64	3055	2.40	5906	2.90	0.29
Schneuer et al <sup>40</sup>	1.22	—	—	—	—	—	—	—
Tennant et al <sup>41</sup>	2.36	—	0.70	—	2.30	—	3.70	1.10
van Nunen et al <sup>42</sup>	2.09	411	1.22	589	2.38	530	2.45	0.45
Wang et al <sup>43</sup>	8.63	—	—	—	—	7356	9.00	—
Yow et al <sup>44</sup>	4.80	—	—	—	—	—	—	2.10

**Table 2. Studies That Reported Mortality Rates Separated by the Presence of Any Other Congenital Comorbidity**

Author	Mortality Rate No Comorbidities, %	Mortality Rate With Comorbidities, %	CL No Comorbidities, %	CL With Comorbidities, %	CLP No Comorbidities, %	CLP With Comorbidities, %	CP No Comorbidities, %	CP With Comorbidities, %
Altunhan et al <sup>25</sup>	0	30.00	—	—	—	—	—	—
Dai et al <sup>28</sup>	5.76	20.10	1.70	13.56	8.88	20.90	3.28	25.09
Druschel et al <sup>29</sup>	0.99	23.48	—	—	1.06	26.10	0.90	21.10
Emanuel et al <sup>30</sup>	2.55	39.81	0	23.10	4.10	51.30	2.60	41.20
Forrester and Merz <sup>32</sup>	0	19.63	—	—	—	—	0	15.80
Hujoel et al <sup>33</sup>	2.93	40.26	—	—	—	—	1.15	44.20
Mc Goldrick et al <sup>36</sup>	2.30	—	—	—	—	—	—	—
Nembhard et al <sup>37</sup>	2.62	52.75	—	—	—	—	3.06	51.10
Ngai et al <sup>38</sup>	1.28	30.59	—	—	—	—	—	—
Ryu et al <sup>39</sup>	0.68	7.55	—	—	—	—	—	—
van Nunen et al <sup>42</sup>	0.35	8.02	0.30	5.30	0.20	13.98	0.77	4.10
Yow et al <sup>44</sup>	0.16	9.69	—	—	—	—	—	—

other 2 groups. This difference may be related to the distribution of comorbidities between the phenotypes. Many common syndromes associated with OFCs, such as Van der Woude syndrome, Pierre Robin sequence, and Velocardiofacial syndrome, are more frequently associated with cleft palate or combined CLP phenotypes.<sup>16,45</sup> Furthermore, many other congenital conditions—ranging from chromosomal disease to limb malformations, to congenital heart disease (CHD)—have been reported more frequently in association with palatal clefts.<sup>16,45–48</sup> Thus, patients with isolated cleft lip may be less likely to have a comorbid condition, thereby reducing mortality rate. Another consideration is that patients with a cleft palate may experience greater feeding difficulty than those with cleft lip alone. Consequent disorders such as malnutrition or aspiration may contribute to decreased survival.

The presence of a comorbidity increased mortality rates in patients with cleft by 7- to 10-fold. Patients with a comorbid cleft had mortality rates ranging from 7.55% to 52.75% compared with 0% to 5.76% for noncomorbid clefts. Apart from OFCs, the most common congenital anomalies among live births include CHD, neurological (neural tube) defects, and Down syndrome.<sup>4,49</sup> Mortality rates for patients with a comorbid cleft seem to supersede reported rates for CHD (10%–12%), neurological defects (15.6%–48.5%), and Down syndrome (7.4%–20.8%).<sup>50–56</sup> Our meta-analysis also demonstrated that the presence of a comorbidity was significantly associated with an increase in odds of mortality regardless of cleft phenotype. These findings highlight the importance of effective coordination between multiple specialist teams, as well as the critical need to ensure patients are fully optimized before surgical intervention.

**Table 3. Mortality Rates by Age Group**

Author	Mortality Rate 0–28 d (Neonatal), %			Mortality Rate 1 mo to 1 y (Infant), %			Mortality Rate 0–1 y, %			Mortality Rate 1–5 y, %			Mortality Rate 5+ y, %		
	C	I	CM	C	I	CM	C	I	CM	C	I	CM	C	I	CM
Abyholm <sup>24</sup>	4.9	—	—	1.63	—	—	—	—	—	—	—	—	—	—	—
Altunhan et al <sup>25</sup>	19.8	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Benjamin et al <sup>27</sup>	7.3	—	—	4.6	—	—	—	—	—	1.4	—	—	0.5	—	—
Druschel et al <sup>29</sup>	—	—	—	—	—	—	8.94	0.99	23.48	—	—	—	—	—	—
Emanuel et al <sup>30</sup>	—	—	—	—	—	—	13.49	2.55	39.81	—	—	—	—	—	—
Forrester and Merz <sup>32</sup>	—	—	—	—	—	—	8.57	0	19.63	—	—	—	—	—	—
Hujoel et al <sup>33</sup>	—	1.63	31.17	—	1.30	9.1	—	—	—	—	—	—	—	—	—
Kang et al <sup>34</sup>	0.94	—	—	2.04	—	—	—	—	—	0.63	—	—	—	—	—
Mc Goldrick et al <sup>36</sup>	6.3	1.4	—	2.5	0.80	—	—	—	—	0.26	0	—	0.24	0.1	—
Nembhard et al <sup>37</sup>	6.63	—	—	6.6	—	—	—	—	—	—	—	—	—	—	—
Ngai et al <sup>38</sup>	6.67	0.9	21.4	—	—	—	—	—	—	—	—	—	—	—	—
Ryu et al <sup>39</sup>	—	—	—	—	—	—	0.93	0.27	3.10	1.19	0.35	3.91	0.18	0.07	0.5
Schneider et al <sup>40</sup>	0.7	—	—	0.3	—	—	—	—	—	0.2	—	—	—	—	—
Tennant et al <sup>41</sup>	2.0	—	—	0.2	—	—	—	—	—	0	—	—	0.2	—	—
van Nunen et al <sup>42</sup>	—	—	—	—	—	—	2.09	0.35	8.02	—	—	—	—	—	—
Wang et al <sup>43</sup>	5.7	—	—	2.93	—	—	—	—	—	—	—	—	—	—	—
Yow et al <sup>44</sup>	2.3	—	—	—	—	—	—	—	—	—	—	—	—	—	—

Results of the age group analysis demonstrated that the odds of mortality were greatest in the neonates followed by infants. Following the first year of life, the odds decreased substantially, with no difference seen in patients between 1 and 5 years of age and those older than 5 years. There was insufficient data to meaningfully stratify different age groups by phenotype or according to the presence or absence of comorbidity. However, other congenital comorbidities have a high risk of mortality in younger patients, with the greatest risk of death seen in many common congenital abnormalities in both the neonatal and infant periods.<sup>40,50,52,56</sup> The impact of both age, malnutrition, and other comorbidities on mortality in patients with CLP represents an interesting direction for future research.

Our findings suggest that changes in the way mortality is reported for patients with cleft may be of value. Within our review, more articles (n = 14) reported mortality among palate-only patients than lip-only patients (n = 8) or those with both (n = 9). Many studies chose to combine patients with CL and CLP into a singular group, “cleft lip with or without cleft palate”—a category not included in our review due to ambiguity. Because we have demonstrated a significant difference in the odds of mortality between CL and CLP, combining them may lead to the reporting of inaccurate mortality rates. Similarly, 5 studies (23.8%) combined the neonatal and infant period into a single “0–1 years of age” group. Our analysis demonstrated this combination is not ideal due to significant differences in odds of mortality between the 2 groups. We recommend that investigators report CL separately from clefts involving the palate, as well as infants and neonates as separate groups to convey more accurate mortality rates.

Other limitations existed for our study. The combination of age groups and cleft phenotypes also restricted the number of studies that could be included in the subgroup analysis. Additionally, worldwide generalizability

may be hard, because only 3 (14.3%) studies described patients in LMICs. Random-effects model analysis of the LMIC data was, therefore, not possible because the low overall number would have resulted in skewed data. Because neonatal, infant, and childhood mortality are all significantly higher in LMICs, the results of this study may underrepresent mortality in patients with CLP on a global scale.<sup>57–59</sup> Furthermore, because the majority of the global CLP disease burden is in LMICs, the lack of published data about cleft mortality from such regions is a significant gap in the literature that should be further investigated.<sup>39</sup> Socioeconomic status of patients was not reported by any studies, prohibiting analysis. This represents a potential confounded and important variable to consider in future studies. Finally, publication dates of selected studies ranged from 1971 to 2023. Due to continued advances in medical technology, neonatal medicine, and pediatric intensive care, mortality rates among all groups included in this study have declined every decade.<sup>60,61</sup> Many pediatric surgical procedures for cardiovascular or gastrointestinal comorbidities were still in their infancy when the older studies we included were published.<sup>60,61</sup> As an example, Mackeprang and Hay<sup>35</sup> reported a cohort between 1956 and 1965, early in the history of pediatric cardiac surgery; a factor that may have contributed to the 20% mortality rate reported in the study. Therefore, the inclusion of these older studies may have led to an overestimation of overall mortality rates among cleft patients and is likely not fully reflective of current mortality. Prospective work investigating cleft mortality would be useful in determining rates that are reflective of modern practice. Due to the lack of granularity and reporting of mortality causes in existing studies, we were unable to discern what proportion of mortality was due to the cleft itself or other syndromic conditions. We recommend that any future work undertaken clearly describes the causes of mortality, as it was poorly reported within the included studies.

Despite these limitations, this is the first study to quantify an overall mortality rate for OFC. The major strength of this study is the meta-analysis of mortality among multiple subgroups of cleft patients, allowing for the recognition of factors that elevate the risk of mortality. Furthermore, the inclusion of multiple large-scale studies resulted in a large patient cohort in each subgroup analysis.

## CONCLUSIONS

This systematic review and meta-analysis evaluated overall mortality in patients with OFC, and also stratified according to cleft phenotype, presence of additional comorbidities, and patient age group. Our results suggest that the presence of comorbidities is a major risk factor for mortality in patients with cleft. Patients with a cleft palate were found to have greater odds of mortality than patients with cleft lip alone, potentially due to more common association of cleft palate with additional congenital conditions. Mortality seemed to be higher in the neonatal and infant periods, which may have important consequences for cleft care algorithms and family counseling. Most available data on cleft mortality come from high-income countries with limited LMIC studies available. To further develop our understanding of cleft mortality, additional emphasis should be placed on conducting large-scale, global studies to accurately reflect the true burden of OFCs generally, and CL/P specifically. We propose reporting CL separately from palatal phenotypes and stratifying age groups into neonates, infants, and children older than 1 year to assist in accurately and comprehensively studying mortality.

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## DISCLOSURE

*The authors have no financial interest to declare in relation to the content of this article.*

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