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Analytical studies in surgery: Cohorts versus cases and controls

Estudios analíticos en cirugía: Cohortes versus casos y controles

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Abstract

Introduction. Analytical observational studies, such as cohort and case-control studies, are fundamental methodologies for generating evidence in surgery when randomized clinical trials are not feasible. Their correct application allows for the investigation of associations between exposures (risk factors, surgical techniques) and clinical outcomes (complications, mortality, functional recovery), contributing to the improvement of evidence-based surgical practice.

Methods. A literature review on cohort and case-control study designs was conducted, focusing on their applications, advantages, limitations, and relevance in surgical settings. Key methodological criteria were analyzed, such as bias control and the estimation of association measures.

Results. Cohort studies allow direct estimation of incidence and relative risk, making them ideal for evaluating common interventions or exposures. In contrast, case-control studies are more efficient for rare diseases or those with a long latency period, although they are more prone to selection and reporting bias. In surgery, both designs have proven useful depending on the clinical context and data availability.

Conclusion. Understanding the methodological differences between cohort and case-control studies is essential for choosing the most appropriate design in surgical research. Their proper use favors the generation of valid and applicable knowledge, particularly in settings where controlled trials are not feasible.

Keywords: research projects; epidemiologic research design; epidemiologic study characteristics; cohort studies; case-control studies; general surgery.

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Resumen

Introducción. Los estudios observacionales analíticos, como los de cohortes y los de casos y controles, son metodologías fundamentales para generar evidencia en cirugía cuando los ensayos clínicos aleatorizados no son factibles. Su correcta aplicación permite investigar asociaciones entre exposiciones (factores de riesgo, técnicas quirúrgicas) y desenlaces clínicos (complicaciones, mortalidad, recuperación funcional), contribuyendo a la mejora de la práctica quirúrgica basada en evidencia.

Métodos. Se realizó una revisión de la literatura sobre los diseños de estudios analíticos, tipo cohorte y casos y controles, enfocada en sus aplicaciones, ventajas, limitaciones y pertinencia en contextos quirúrgicos. Se analizaron criterios metodológicos clave, como el control de sesgos y la estimación de medidas de asociación.

Resultados. Los estudios de cohortes permiten estimar directamente la incidencia y el riesgo relativo, siendo ideales para evaluar intervenciones o exposiciones frecuentes. En contraste, los estudios de casos y controles son más eficientes para enfermedades raras o de largo período de latencia, aunque más propensos a sesgos de selección e información. En cirugía, ambos diseños han demostrado ser útiles según el contexto clínico y la disponibilidad de datos.

Conclusión. Comprender las diferencias metodológicas entre estudios de cohortes y de casos y controles es esencial para elegir el diseño más adecuado en investigación quirúrgica. Su correcta utilización favorece la generación de conocimiento válido y aplicable, particularmente en escenarios donde los ensayos controlados no son viables.

Palabras clave: proyectos de investigación; diseño de investigaciones epidemiológicas; características de estudios epidemiológicos; estudios de cohortes; estudios de casos y controles; cirugía general.

Introduction

While controlled clinical trials are considered the gold standard of research designs because they provide the most convincing evidence of the relationship between exposure and outcome, in the field of surgical specialties, they face ethical difficulties and greater risks of bias. Therefore, we are forced to use non-experimental studies, which are those in which the researcher does not assign or alter the exposure being evaluated [1]. A good alternative is analytical studies, which seek to evaluate the association between exposure and an outcome, whether a disease or another health outcome.

Before beginning any research, it is essential to carefully plan every detail of the project, starting with defining the most appropriate design to achieve the proposed objective. For observational studies, which include analytical studies, it is recommended to follow the recommendations of the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) Guidelines [2].

The objective of this new publication in the Research and Surgery series was to present two alternatives for surgical research, focusing on the design, methods, advantages, and limitations of each, with the aim of stimulating the development of this type of studies among research groups in surgical fields.

Generalities

Cohort and case-control studies are considered observational, analytical, and longitudinal [3,4]. First, because the researcher does not perform any "intervention" or manipulation of the independent variables; second, because they evaluate a possible association between the exposure and the event of interest (a presumed cause-effect relationship), an association that can be established between two or more variables; and third, because observations are made over time.

Among analytical studies, temporality makes the difference. In cohort studies, the exposure is the starting point to evaluate its possible effect (called an event or outcome) [5]; in contrast, in

case-control studies, the effect is the starting point to search for a possible exposure [6], while in cross-sectional studies, the exposure and outcome are measured in parallel.

Cohort studies

A cohort refers to a group of people who share a defined characteristic and are followed over time [7]. In this type of study, it is very important to define the source population from which the cohorts will be drawn, as well as the inclusion and exclusion criteria, in order to select subjects without the event of interest to be evaluated, but with the risk of developing it. The cohorts of exposed and unexposed individuals must be similar in all aspects, apart from the variable being studied, and they must not present the outcome at the start of the study [4]. Measurement of exposure can be dichotomous (exposed versus unexposed) or categorical (by level, magnitude or time). Ideally, within international standards, tests to identify events should be simple, safe and inexpensive, without forgetting that any measurement must be as objective and exhaustive as possible [8].

Depending on the relationship between the time the study begins and the diagnosis of the disease, a cohort study can be prospective or retrospective [8]. The first type is when the researcher defines the cohorts (those exposed or not exposed to a possible risk factor) and follows them over time to identify the onset of the outcome (disease or mortality in each group), that is, the start of the study occurs before the events actually occurred. The second type is when the exposure and the outcome have already occurred at the time the study begins, but the identification of the cohorts is based on an event that occurred on a clearly established (previous) date, so good records are required to capture the information. A third type is ambispective (ambidirectional), in which data are collected prospectively and retrospectively from the same cohorts [4].

On the other hand, the cohort can be fixed or dynamic [8]. A fixed cohort only includes subjects selected at the beginning of the study, meaning the inclusion date is the same for all individuals. A dynamic cohort allows for inclusion of subjects as the study progresses, as they are identified, so that the inclusion date is different for each individual. In theory, this option has a lower risk of selection bias because individuals are included at the same stage of disease progression.

The validity of the results is achieved with complete and accurate measurement of the values for each variable. Therefore, it is important to follow up on as many subjects as possible until the end of the study, although losses of up to 20% are acceptable [4,7]. Follow-up in a cohort ends when the event of interest occurs, the subject dies or withdraws from the study, is lost to follow-up, or the study ends.

Case-control studies

Case-control studies are a cost-effective strategy for identifying risk factors and generating hypotheses for further study [6].

Cases must be identified, clearly defining the disease and the criteria that individuals with the event must meet (effect or outcome) to be included in the study [9]. When available, it is recommended to use a standardized definition accepted by well-established research societies or groups, using the best diagnostic techniques, to avoid disagreements in case selection and reduce false positives and false negatives.

The timing of the disease is also important. Cases can be prevalent when identified from the beginning of the study, or incident cases, which are those that "appear" during follow-up. Several authors recommend prioritizing incident cases because they are more similar and consistent with the current time point of the study [3].

The selection of controls is possibly the most important methodological aspect, since they must come from the same population as the cases and be representative, to provide internal validity to the study [3,5]. They must be similar to the cases in most aspects, with the exception of exposure. However, conceptually, controls should have the same probability of having been exposed as cases and the same probability of being selected for the study, so sampling using probability or random

methods is recommended [9,10]. People with related diseases that positively or negatively affect exposure should be excluded from the controls [3,10].

Depending on the disease being studied, controls can be selected from hospital or community settings. In the latter case, depending on the course of the disease, they could come from the neighborhood, family or circle of friends, school, or workplace. To do this, it is important to keep in mind the development of the project, which involves identifying the exposure and outcome, the feasibility of long-term follow-up, and the ease of contacting controls in the future. As in any study, it is important to explicitly define any instrument, scale, score, or value (cutoff point) to be used to avoid errors and bias.

In the event that the number of cases is insufficient to achieve a well-powered statistical analysis, statistical efficiency can be improved by increasing the sample size. This is achieved by including more controls, up to a maximum of four controls per case. It has been shown that above this number, the power of the study increases very little, but costs increase disproportionately [5,9,11].

Cases and controls must have characteristics of representativeness, simultaneity, and homogeneity [6]. Representativeness means that cases must represent all existing cases at a given time and that those selected as controls must represent subjects who may become cases within the same population; simultaneity means that controls must be chosen from the same time the cases were diagnosed; and homogeneity means that controls must be selected from the same cohort from which the cases originate.

Statistical analysis

Cohort studies allow for the calculation of association measures, which are epidemiological indicators of the strength of the association between an exposure (possible cause) and an outcome (disease). They can be expressed as probabilities (risk) or rates (incidence). Risk reflects the ratio of subjects who experience the outcome to the total number of subjects included in the study; incidence reflects the speed at which the outcome occurs per unit of time [4]. Thus, incidence or incidence rate corresponds to the number of new cases detected in a group over a given period. These measures can be effect measures, based on the calculation of a quotient such as the absolute risk (incidence rate ratio) (AR) and the relative risk (RR), or impact measures, based on differences, such as the absolute risk reduction (ARR), the relative risk reduction (RRR), and the number needed to treat (NNT) [7].

On the other hand, odds is a ratio between two mutually exclusive events. In research, it corresponds to the ratio between the occurrence or non-occurrence of an event, or its probability [5]. In case-control studies, to evaluate the association between two variables, the probability of exposure between participants with the disease and "healthy" participants (without the outcome) is compared; therefore, it is called odds ratio (also called odds ratio, disparity ratio, advantage ratio, cross-product ratio, or relative opportunity ratio, among others) [6]. When the prevalence of a disease is low (less than 5%), the odds ratio (OR) approximates the RR used in cohort studies [10]. The inclusion of confidence intervals and the p value helps to obtain an idea of the precision of the finding and the statistical significance. Due to their characteristics, in case-control studies it is not possible to estimate relative risks or attributable risks [11].

Bias control

In cohort studies, the greatest challenge is long-term follow-up. Therefore, the design should establish the same guidelines for both groups, including the frequency and periodicity of assessments (visits), methods, data sources, and tools (questionnaires, surveys, or instruments). These guidelines should be administered by observers who are unaware of the study group of each subject, to avoid over- or under-control of one cohort (observation, reporting, or measurement bias) [12].

When individual syndromes or symptoms are assessed without an objective examination, internationally accepted definitions should be used. If the information comes from previously

established registries, there may be a lack of data standardization or variability in diagnostic criteria, or the registries may not be appropriate for the study objectives [8]. Therefore, it is important to periodically assess individuals in each cohort.

In case-control studies, there is a greater risk of selection bias when individuals in one of the groups are included or excluded due to a characteristic related to the exposure; as mentioned in a previous article in this series, Berkson and Neyman biases are prominent [3,12,13]. Selection bias can be controlled through matching, but it should be remembered that from that point on, the effect of the variable being matched cannot be studied (because by definition, cases and controls are the same), and that the flexibility of statistical analysis is reduced because it is necessary to use techniques for paired data [6,9].

The temporal sequence of case-control studies requires obtaining information about past exposure, making them more susceptible to information biases, such as memory bias, recall bias, and interviewer bias [3,12]. Therefore, it is necessary to try to obtain information from objective records, such as medical records or reports of previous diagnostic studies, and to design well-structured surveys or questionnaires, since biological measurements can only be incorporated into the study in rare cases.

Case-control studies are more likely to be confounded, a condition that can be adjusted for using multiple logistic regression analysis or a stratified Mantel-Haenszel analysis; when the crude and adjusted estimates are similar, the results are more reliable [3,10,11]. Finally, a propensity score can also be applied, and the goodness of fit of the models should be assessed using tests such as that of Hosmer & Lemeshow [3,5].

Advantages and limitations of each design

There is no perfect design, so it is ideal for researchers to understand the limitations of each in order to choose the design that best addresses their research question.

Cohort studies seek to determine the association between an exposure and an outcome by estimating risks, understanding the clinical course, identifying protective factors, and estimating prognosis or survival. Their advantages include [7]:

- It is the only method for estimating incidence.
- It is the ideal design for studying the natural history of a disease.
- They allow for the study of causality because they show the temporal sequence between exposure and outcome.
- They help study rare exposures or fatal diseases.
- They can simultaneously evaluate multiple outcomes potentially associated with an exposure.
- Prospective designs minimize measurement errors.

Therefore, they are not useful for studying rare events, as they would require a very large sample size or a prolonged course of the disease, which would require very long follow-up, resulting in high costs in money and time.

Cohort studies are less subject to bias when the population is selected based on exposure [9]. Their main limitation is that losses to follow up can invalidate the results when the proportion of losses differs between cohorts; if this occurs, an attempt should be made to obtain as much information as possible on the characteristics and causes of the losses [7].

There are several advantages to case-control studies, including [6]:

- They are relatively simple.
- They offer a greater level of information because more patients with the same disease can be studied.
- They allow for the simultaneous assessment of multiple exposures or risk factors, especially those that are rare in the general population, and their interactions.
- They require fewer subjects, for whom the assessment is more in-depth.

- They estimate the true relative risk if the principles of representativeness, simultaneity, and homogeneity are met.
- They are more efficient: they generally take less time to complete since the outcome has already occurred.
- They have lower costs.

With this in mind, case-control studies are recommended for rare conditions that occur in outbreaks or with long latency periods; conversely, they are not indicated for infrequent exposures.

The major limitation of case-control studies is that they do not allow for calculating prevalence, since the proportion of people with and without the event is fixed, determined by the researcher during the study design phase using the case-control ratio. They also do not allow for establishing the temporal sequence between exposure and outcome, nor for determining other possible effects of an exposure, because they are based on a single outcome [6]. The main disadvantage is the frequency of biases, especially selection bias, but also information bias [12].

Conclusions

Observational analytical studies, particularly cohort and case-control studies, are fundamental tools for clinical research in surgery. Each has strengths and limitations that must be carefully considered when formulating a research question, designing a study, and analyzing its results.

Cohort studies offer the advantage of establishing a clear temporal sequence between exposure and outcome, which strengthens causal inference. They are especially useful in evaluating prognostic factors, postoperative complications, or the long-term effects of surgical interventions. However, they require more time, resources, and follow-up, which can make their implementation difficult in some surgical settings.

On the other hand, case-control studies are more efficient for investigating rare or late-onset events, being faster and less expensive. However, they are more prone to bias, especially selection and reporting bias, and do not allow for direct calculation of true incidences or relative risks.

In the surgical field, where randomized clinical trials are often not feasible for ethical or logistical reasons, well-designed observational studies represent a valid alternative for generating evidence. The choice between a cohort or case-control design should be guided by the nature of the clinical problem, data availability, and the methodological resources of the research team.

In conclusion, a thorough understanding of the methodological principles of each type of study allows for the selection of the most appropriate design and ensures the validity of the findings in the context of surgical practice.

Compliance with ethical standards

Informed consent: This study is a literature review, and as such, there is no need for informed consent or Institutional Ethics Committee approval.

Conflicts of interest: The authors declared that they have no conflicts of interest.

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- Conception and design of the study: Mónica Bejarano, Patrizio Petrone.
- Acquisition of data: Mónica Bejarano, Patrizio Petrone.
- Data analysis and interpretation: Mónica Bejarano, Patrizio Petrone.
- Drafting the manuscript: Mónica Bejarano, Patrizio Petrone.
- Critical review and final approval: Mónica Bejarano, Patrizio Petrone.

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